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To evaluate the level of agreement between two self-reported medication adherence scales and prescription refill records in older adults

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MEASUREMENT OF ADHERENCE TO ANTIHYPERTENSIVE MEDICATIONS IN OLDER ADULTS USING SELF-REPORT METHOD COMPARED TO PRESCRIPTION REFILL RECORDS

A Thesis submitted in partial fulfillment of the requirements for the degree of Master in Pharmaceutical Sciences at Virginia Commonwealth University.

by

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Abstract

Measurement of Adherence to Antihypertensive Medications in Older Adults Using Self-report method compared to Prescription Fill records

By Priyanka Parshuram Kakad, B. Pharm., MS

A Thesis submitted in partial fulfillment of the requirements for the degree of Masters of Science in Pharmaceutical Sciences at Virginia Commonwealth University
.

Virginia Commonwealth University, 2009

Major Director: Dr. Patricia W. Slattum, PharmD, PhD
Director of Geriatric Pharmacotherapy program, Associate Professor and Geriatric Specialist, Department of Pharmacy

Objective:
To evaluate the level of agreement between two self-reported medication adherence scales and prescription refill records in older adults.
Design:
Cross-sectional study
Setting:
Imperial Plaza; a retirement community located in Richmond, Virginia.

Participants:
32 independent-living older adults, taking anti-hypertensive medications and filling their prescriptions at on-site Plaza Professional Pharmacy were recruited in the study.

Methods:
Participants' 6 months refill records were obtained and Medication Possession Ration (MPR) was calculated. Participants were interviewed using Morisky Medication Adherence Scale (MMAS) & Brief Medication Questionnaire (BMQ). Kappa (*k*) statistics was used to evaluate the level of agreement.

Results:
Poor level of agreement was found between refill records and MMAS (*k*=-0.004), refill records and BMQ belief screen (*k*=-0.09), regimen screen ((*k*=-0.09), and recall screen (*k* =-0.004). Strong agreement was found between MMAS and BMQ regimen screen (*k*=0.79) and recall screen (*k*=0.87 resp.)

Conclusion:
Self-reported measure of adherence exhibited poor agreement with prescription refill records.

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CHAPTER 1 INTRODUCTION

Background

Adherence to medications is defined as "the extent to which a person's behavior in taking medication, following a diet, and/or executing lifestyle changes; corresponds with agreed recommendations from a health care provider" (World health organization, 2003; Osterberg & Blaschke, 2005). In order to adhere to medications, a patient has to play an active and voluntary role in the ongoing treatment process. The term "compliance" is often used interchangeably with "adherence" to describe patient's medication-taking behavior. However, the term "compliance" has come into disfavor because it suggests that a patient is passively following a doctor's orders, rather than actively collaborating in the treatment process. The term to describe medication-taking behavior has been discordant in the past literature with a move away from compliance towards adherence (World health organization. adherence to long-therapies: Evidence for action. geneva.2003). Understanding a patient's medication-taking behavior is an intriguing and complex phenomenon.

It is estimated that failure to adhere to medication regimens in the United States results in 125,000 deaths and may cost about $100 billion annually (Hughes, 2004; Krueger, Berger, & Felkey, 2005; Vermeire, Hearnshaw, Van Royen, & Denekens,

2001). Consequences of non-adherence are profound, such as ineffectiveness of treatment and worsening of disease progression resulting in poor outcomes. Severe disease complications may lead to patient hospitalization, rehospitalization and emergency department visits, which in turn increase the economic burden. Very importantly, medication non-adherence may affect the patient's health related quality of life (Balkrishnan & Jayawant, 2007; Hughes, 2004).

The prevalence of medication non-adherence ranges from 13 to 93%, with an average rate of 40%, and this range encompasses all ages and ethnic groups (Bond & Hussar, 1991). The non-adherence rate with medications for acute disease conditions ranges from 23 to 40%, while this rate ranges from 40 to 75% for long term or chronic medications (Haynes et al., 1980). This variation is due to inclusion of different populations, type of study design (*e.g.* observational study versus clinical trial), medication class, method of adherence measurement, source of data, and definition of adherence used (Haynes et al., 1980). Such high rates of non-adherence suggest that approximately half of the patients with chronic diseases have problems following their prescribed regimen and that they may not achieve optimal clinical benefit. Chronic illnesses are more common among older adults and are one of the leading causes of death and disability in this population (Salzman, 1995).

Adherence is simultaneously influenced by several factors and studies over the past three decades have identified a number of these factors affecting medication adherence (Balkrishnan & Jayawant, 2007; Hughes, 2004). The World Health Organization in 2003 suggested that medication adherence can be determined by interplay of five sets of

factors, termed as "dimensions" viz. social and economic, health care system, condition-related, therapy-related, and patient-related factors (World health organization. adherence, 2003).

Social and economic factors such as poor literacy level, poor social support, family instability, limited access to health care, cost of the medications and homelessness are the most consistently reported factors to impact medication adherence (Krousel-Wood, Hyre, Muntner, & Morisky, 2005; Krueger et al., 2005). People who have social support from family, friends, or caregivers to assist with medication regimens have been found to have better adherence to treatment. Medication beliefs, level of education and understanding the importance of the treatment and the treatment instructions are also important factors that affect medication-taking behavior (Gatti, Jacobson, Gazmararian, Schmotzer, & Kripalani, 2009; Horne & Weinman, 1999). Patients aged 65 or above, who had more negative beliefs about medications, had 2.1 times greater odds of low medication adherence compared with patients with less negative beliefs (Gatti et al., 2009).

The quality of the health care provider-patient relationship is one of the most important *health care system-related factors* that affects medication adherence along with poor access or missed appointment and lack of continuity of care. It has been shown that a good relationship between the patient and a physician, nurses or pharmacists, which features encouragement and reinforcement from them, has a positive impact on adherence (Haskard Zolnierek & Dimatteo, 2009; Krueger et al., 2005; Vik, Maxwell, & Hogan, 2004; Vlasnik, Aliotta, & DeLor, 2005).

Two of the most important *disease condition-related factors* contributing to poor adherence are undoubtedly the asymptomatic and lifelong nature of the disease (Krousel-Wood et al., 2005; Krueger et al., 2005). Prevalence of non-adherence is higher in case of chronic disease conditions than acute disease conditions (Krueger et al., 2005). Medications have to be taken indefinitely for many chronic illnesses, and adherence to such treatment regimens often declines significantly over time. Due to lack of immediate benefit of the therapy for many disease states, some older adults do not adhere to their treatment (Krousel-Wood et al., 2005; Krueger et al., 2005).

Therapy-related factors affect medication adherence due to the complexity of medication regimen (no. of meds and no of daily doses), duration of therapy, lack of immediate benefit of therapy, medications with social stigma attached to it and actual or perceived unpleasant side effects of the medications. All of these factors lead to medication non-adherence (World Health Organization, 2003; Krousel-Wood et al., 2005; Krueger et al., 2005).

Many *patient-related factors* such as lack of knowledge about the disease and the reasons why medication is needed, lack of motivation, low self-efficacy, forgetfulness and substance abuse are associated with poor medication adherence. (Osterberg & Blaschke, 2005; Vermeire et al., 2001) Some patient-related physical factors such as vision or hearing impairment, cognitive impairment, limited dexterity, and swallowing problems also leads to medication non-adherence.

According to the 2000 census, the number of people aged 65 and older in the United States was estimated to be 35 million and this population accounts for one-third of all

health expenditures including prescribed drugs (Raehl, Bond, Woods, Patry, & Sleeper, 2006). Medication non-adherence accounts for 26% of older adult hospital admissions, nearly 1/4 of nursing home admissions and 20% of preventable adverse drug events among older adults in community settings (Donovan, 1995; Vermeire et al., 2001). Thus, adherence is particularly challenging in older adults who often have multiple medical conditions to manage with a high number of concurrent medications (Hughes, 2004). The consequences of non-adherence may be more serious, less easily detected, and less easily resolved in older adults than in a younger age group (Hughes, 2004). In older people, perceptions of illness and poor comprehension of the role of medicines in the management of long-term conditions can lead to intentional non-adherence with medications (Gatti et al., 2009; Lowry, Dudley, Oddone, & Bosworth, 2005).

Hypertension is an especially common chronic illness. According to the National Center for Health Statistics it is present in 26.7% of the United States population between ages 20 to 74 (National Center for Health Statistics, 2006). The prevalence of hypertension among older adults aged 60 and above rose from 58% to approximately 67% over the 10 years (Ostchega, Dillon, Hughes, Carroll, & Yoon, 2007). The seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) has identified that low adherence to prescribed antihypertensive medications is potentially a major barrier to adequate blood pressure control and has referred to it as "America's other drug problem" (*The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure).*

There is a positive, continuous, consistent relationship between blood pressure and risk of cardiovascular events independent of other risk factors. Cardiovascular diseases are preventable and primary prevention studies have shown that antihypertensive agents, including diuretics, β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers are associated with a 30% to 40% reduction in the incidence of cardiovascular diseases (Vermeire et al., 2001). However, the large reductions in risks associated with cardiovascular diseases seen in clinical trials with these drugs may not translate into better prognoses in the "real-world" setting if patients have trouble adhering to their prescribed regimens. Non-adherence with antihypertensive medications leads to suboptimal blood pressure control, high risk of cardiovascular diseases, more accelerated and severe hypertension, more hospitalizations and premature death and eventually potentially greater health cost.

Potential reasons for poor medication taking behavior, particularly during antihypertensive therapy, are cost of medication and related care, unclear instructions, failure of physician to increase or change therapy to achieve blood pressure goals, inadequate or no patient education, lack of involvement of patient in treatment plan and some therapy related factors like side effects of medication and complexity of dosing regimen (Burnier, 2006; Patel & Taylor, 2002). Effective interventions are needed to equip health care providers with tools to improve antihypertensive medication adherence among older adults.

Poor medication adherence has reached crisis proportions in the United States leading to significant economic cost. Thus it is imperative to understand the factors

affecting medication adherence and ultimately to develop effective interventions to improve adherence (Banning, 2008).

Studies have explored definition, factors associated with nonadherence, predictors, and consequences of nonadherence. However lack of a "gold standard" measure to assess medication adherence continues to impose challenges and is the biggest clinical hurdle that is necessary to target the consequences of medication non-adherence (Balkrishnan & Jayawant, 2007; Osterberg & Blaschke, 2005).

There are both direct and indirect methods of measuring medication adherence. The direct method includes biological assay where the presence of a drug or its metabolite in a biologic fluid provides confirmation that the patient has received a dose of medication within some period of analysis. The indirect methods of measuring medication adherence are more frequently reported in the literature and include patient interviews, diaries, self-report questionnaires, pill counts, pharmacy records, prescription claims, clinical outcomes, and electronic monitoring.

All the current methods used to measure adherence have some advantages and disadvantages. When choosing a method for identifying patients who are non-adherent for an intervention or assessing the outcomes of an intervention to improve adherence for a particular patient population, it is crucial to evaluate if adherence measured by various methods agree with each other in the population of interest.

Objective and Specific Aims

The main objective of this study was to evaluate the agreement between two self-report methods, Morisky Medication Adherence Scale (MMAS) and Brief Medication Questionnaire (BMQ), and prescription refill records to identify an appropriate tool to measure adherence in independently living older adults with hypertension. Both the MMAS and BMQ have been previously demonstrated to be reliable measures to assess medication adherence and they are among the most practical approaches available to measure adherence. However, a gold standard method to measure adherence in older adults has not been identified.

The study has the following specific aims:

Specific Aim 1: Measure adherence to antihypertensive medications using MMAS in older adults.

Specific Aim 2: Measure adherence to antihypertensive medications using BMQ in older adults.

Specific Aim 3: Measure adherence to antihypertensive medications using prescription fills records in older adults.

Specific Aim 4: Compare the adherence rate measured by MMAS and prescription fill records to evaluate agreement between them.

Specific Aim 5: Compare the adherence rate measured by BMQ and prescription fill records to evaluate agreement between them.

Specific Aim 6: Compare the adherence rate measured by MMAS and BMQ to evaluate agreement between them.

Significance of the study

The U.S Census Bureau reports that by 2030, older adults will account for 20% of the total U.S. population. The prevalence of hypertension among older adults rose from 58% to 67% in past 10 years. Non-adherence to antihypertensive medications remains a global problem and imposes financial burden in terms of direct and indirect health care costs. Promoting patient adherence is a major clinical hurdle that is necessary to decrease cardiovascular morbidity and mortality (Ostchega et al., 2007; Rizzo & Simons, 1997). Several studies have previously implemented MMAS and prescription refill records methods to assess adherence and to understand the underlying reasons for non-adherence(Wetzels, Nelemans, Schouten, van Wijk, & Prins, 2006; Wu, Moser, Chung, & Lennie, 2008; Zeller, Schroeder, & Peters, 2008). However, lack of a "gold standard" measure to assess medication adherence continues to impose challenges (Vik et al., 2004). It is important to address some of the issues in the currently under-researched realm of medication adherence in older adults.

This will be one of the few studies to include older adults exclusively. The average age of the residents of the Imperial Plaza is 84 years, thus the results of the study and the qualitative observations drawn from the participant interviews will contribute to understanding the patterns of adherence and non-adherence in older adults. Evaluating agreement between self-report and prescription refill records to assess medication adherence in older adults will be an important step towards identifying an appropriate tool to evaluate adherence interventions targeted to older adults. The interview based self-report method will facilitate the qualitative observations on older adults' medication-

taking behavior in detail. The self-report questionnaires used in this study have been developed and validated for use in hypertensive populations. Adherence rate for all the antihypertensive medications will be assessed in older adults. The comparison of adherence rates obtained through these three methods will help establish the reliability and feasibility of these methods in independent living older adults congregate living setting. A multi-method approach that combines feasible self-reporting of medication-taking behavior and reasonable objective measures is the current state-of-the-art in measurement of adherence behavior (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Kripalani, Yao, & Haynes, 2007).

CHAPTER 2 LITERATURE REVIEW

This chapter provides a detailed description of the methods available to identify and quantify medication adherence. Some observational studies that compared different methods of medication adherence are discussed. As mentioned earlier, the term "compliance" is often used interchangeably with "adherence" in the literature. This study particularly focuses on medication adherence, however as the majority of the studies discussed here use the term compliance; these studies are also included in the literature review.

To understand the problem of treatment adherence and assess the effectiveness of interventions to improve adherence, it needs to be accurately measured (McDonald, Garg, & Haynes, 2002). There are both direct and indirect methods to measure medication adherence.

The direct method includes biological assay where the presence of a drug or its metabolite in a biologic fluid provides confirmation that the patient has received a dose of medication within some period of analysis. Though this is an accurate measure of the concentration of drug in body fluids, it is intrusive, expensive, and impractical in a non-research setting. In addition, this method does not provide information about the type of non-adherence (intentional or unintentional) and does not detect "white-coat adherence"

where the patient may be non-adherent until shortly before a clinic appointment and return to non-adherent behavior after the clinical visit (Farmer, 1999; Lowry et al., 2005; Vik et al., 2004).

Biologic markers are nontoxic, stable, easily detected compounds that can be added to medications. It is impossible to quantify adherence and this method has the same shortcomings as biologic fluid drug levels (Farmer, 1999).

During direct patient observation patients are closely monitored receiving their medications. Direct patient observation is feasible during clinical trials and some institutional settings. Deliberate non-adherent can feign the swallowing the medication and then remove it from their mouth when they are no longer being observed. This method is not practical during out-patient settings (Farmer, 1999). These methods are described in the Table 2.1

Table 2.1: Direct Methods to Measure Medication Adherence

Method	Advantages	Disadvantages
Drugs level in biologic fluids	Provides a confirmation that the patient has received a dose	1) Data limited to recent use 2) Patient-specific kinetic variation 3) White-coat adherence
Biologic markers	1) Nontoxic 2) Stable 3) Easy detection	1) Data limited to recent use 2) Limited to clinical trials only
Direct patient observation	Detail information about adherence pattern	1) Impractical in outpatient setting

The indirect methods of measuring medication adherence are more frequently reported in the literature and include patient interviews, diaries, pill counts, pharmacy refill records, prescription claims and electronic monitoring and self-report questionnaire (Farmer, 1999).

Pill count is simply counting the number of dosage units that the patient has not taken by the scheduled appointment or clinic visit. The returned dosage units are counted and compared with the number of units received by the patient in the most recent prescription and the length of time since the medication was dispensed. It is a simple and inexpensive method to calculate adherence rate (Haynes et al., 1980). However, the accuracy of pill counts in estimating actual adherence with a medication regimen can vary widely. Patients may deliberately not return their medications, some know that the purpose of their pill counts is to determine their adherence, and they may not return all the pills to hide their errant behavior. Information on nature of the adherence problem (e. g., the pattern of missed doses) or the reasons for the problem (e.g. side effects) cannot be obtained through pill counts (Hansen et al., 2009; Haynes RB, Taylor DW, Sacket DL., 1979; Haynes et al., 1980)

Patient kept diaries is also an inexpensive and simple method. It provides information on number and days the pills are missed by a patient. Patient may be able to document the reason for non-adherence. However, the patient may not truthfully report the drug intake and patient has to remember to document what pills he forgot to take. Direct patient observation can be done in clinical trials and some institutional settings.

However this method is not practical in outpatient settings (Dunbar J., 1980; Farmer, 1999).

Medication Event Monitoring System (MEMS) cap has been widely used in studies involving electronic monitoring devices. These electronic devices contain a microprocessor that records the time and date that the patient obtains a dose of medication by detecting when a prescription vial or pill box is opened; a pill is removed from a blister pack or pill ring. Electronic monitoring has significant advantages over biologic markers and self-report methods in providing continuous, reliable data on actual medication use. It is useful in determining the precision with which the patient adheres to the prescribed regimen (Banning, 2009). The data provided by these devices can determine whether the patient consistently misses the afternoon dose of the 3-times-daily regimen, for example, or the patient misses doses sporadically. However there is a possibility of patient accidently or purposefully actuating the medication container without taking the medications.

Pharmacy records and prescription claims are used to estimate non-adherence and they are often readily available and provide an "economical approach". This is the frequently used objective methods for measuring medication non-adherence. Adherence rate is calculated by assessing refill gaps. Pharmacy refill records allow the researcher to study premature discontinuation of therapy. Prescription refill records give (DiMatteo, 2004; DiMatteo, 2004; Kripalani et al., 2007; Steiner & Prochazka, 1997; Vik et al., 2004)

Self report methods have been used in 25.5% of the studies that measured non-adherence (DiMatteo, 2004). Though self reporting measures do not provide an accurate measure of when and how patients take their medications, it still provides a "relative understanding of the patient on the adherence dimension" and is inexpensive. (Horne & Weinman, 1999) It is suggest that self reporting measures are good measures when the objective of the study is to just identify non-adherers (Haynes RB, Taylor DW, Sacket DL., 1979). The most widely used self reporting measures of non-adherence are Morisky Medication Adherence scale (MMAS) (Morisky, Ang, Krousel-Wood, & Ward, 2008), Medication Adherence Scale (MAS) (MacLaughlin et al., 2005), and Reported Adherence to Medication (RAM) scale. All these scales are based on the classification of non-adherence as intentional and unintentional. The questions of this scale measure patient's non-adherence rate relating to forgetfulness and carelessness in taking medications. Brief Medication Questionnaire (BMQ) is another widely used tool in the practice settings. BMQ screens patients for non-adherence using regimen screen, belief screen, recall screen and access screen (Svarstad, Chewning, Sleath, & Claesson, 1999). These methods are described in Table 2.2.

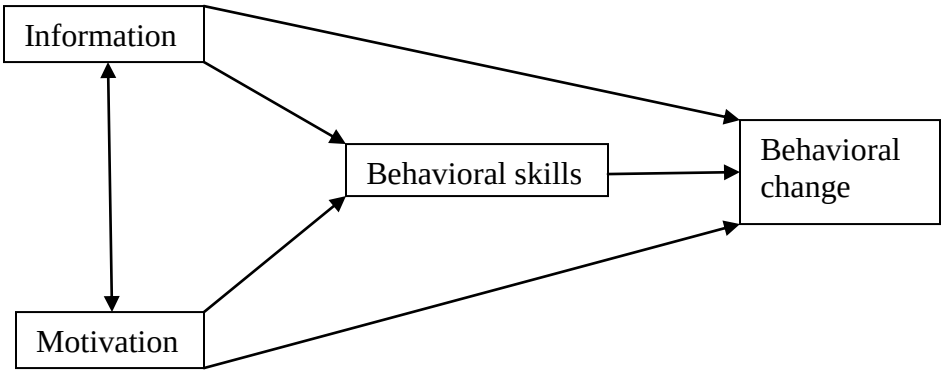
Table 2.2: Indirect Methods to Measure Adherence

Method	Advantages	Disadvantages
Patient-kept diary	Self-report method with regimen data	1) Potential for overestimation 2) Patient must return diary
Adherence questionnaire	1) Easy to administer 2) May explain patient behavior	1) Lack of continuous data 2) Accuracy is instrument dependent
Pill count	1) Easy to use 2) Inexpensive	Patient may forget or alter unused portion
Prescription refill records	1) Noninvasive 2) Long-term data 3) Large populations	1) Knowledge of database required 2) No information on the actual consumption
Medication Event Monitoring System (MEMS)	Precise data on regimen adherence	1) Expensive 2) Inconvenient 3) White-coat adherence

Various models have been established in the past literature like health belief model, theory of reasoned action, self-efficacy theory, and theory of planned behavior to study medication adherence (Lau et al., 2008). As evidenced from the literature review, no single theory can explain medication non-adherence adequately (World Health Organization 2003). The health belief model is based on the understanding that a person will take a health-related action if person feels that a negative health condition can be avoided, if a person has a positive expectations that by taking recommended action or medication he will avoid a negative health condition and if a person believes that he can successfully take a recommended health action (Pires & Mussi, 2008; Stafford, Jackson,

& Berk, 2008). Patient's belief about the necessity of the medications versus their concerns about potential adverse effects plays very important role in self-management of medications. Foundation model for medication adherence as defined by World Health Organization has these three components such as information, motivation and behavioral skills (World health organization. adherence to long-therapies: Evidence for action. geneva.2003). Figure 2.1 depicts the foundational model for medication adherence as described by World Health Organization.

Figure 2.1: Foundational Model for Medication Adherence



MMAS measures patient's intentional and non-intentional adherence. This scale can assess treatment-related attitude and behavior problems that the patient may be facing can be immediately identified and health care providers may provide reinforcement and advise such that the patient can take positive steps early to address these issues (Morisky, Green, & Levine, 1986; Morisky et al., 2008). BMQ has been previously used to examine

the relationship between beliefs about medications, health literacy and self-reported medication adherence. BMQ measures patient's beliefs and access to the medications. As these components help patient adhere to the treatment, this scale is helpful in screening patients who are non-adherent to their treatment (Svarstad et al., 1999). Thus these two scales fit well into the concepts derived from health belief model and foundational model for medication adherence.

When choosing a method for identifying patients who are nonadherent for an intervention or assessing the outcomes of an intervention to improve adherence for a particular patient population, it is crucial to evaluate if adherence measured by various methods agree with each other in the population of interest. For the purpose of this study adherence to antihypertensive medications was measured using self-report method and prescription refill records. As mentioned earlier MMAS and BMQ are one of the most useful and practical self-report measures, hence these two measures were used to measure adherence in older adults.

The objective of this literature review was to review the studies that have compared different methods to measure medication adherence in hypertensive patients.

Adherence studies comparing different methods to measure adherence

Search Methods

Computerized database searches of English-language articles were conducted in MEDLINE, and Cochrane Library. Search terms used included *hypertension, medication adherence, medication compliance, patient compliance, patient adherence, and self-report and prescription data, prescription refill records.* The retrieved citations' abstracts were reviewed for relevance. Additional references were obtained from cross-referencing the bibliographies of selected articles.

Cook et. al. evaluated the concordance among three self-reported measures such as BMQ, Medication Adherence Survey (MAS) and the Medical Outcomes Study (MOS) instruments and pharmacy refill. From five primary care physicians' office 139 patients aged between 20 and 91, with one or more of following chronic conditions were enrolled in the study: diabetes mellitus, hormone replacement therapy, hypercholesterolemia, hypertension and hypothyroidism were included in the study. Moderate correlations of 0.234, 0.261, and 0.213 were found between refill records and the MAS, MOS, and BMQ belief screen respectively. Overall high rate of adherence rate was observed in this population. The study findings underscored the difficulty in both assessing patient's medication-taking behavior and assessing and comparing the results of adherence research (Cook, Wade, Martin, & Perri, 2005).

Nina van de Steeg et. al. performed a validation study of two established questionnaires for the measurement of medical adherence of patients treated with

antihypertensive drugs: MMAS and Medication Adherence Report Scale (MARS-5). It was concluded from this study MMAS the MARS-5 cannot be recommended to be used to measure adherence to antihypertensive drugs in the primary care setting at this point. This study underlined the necessity to validate questionnaires in a specific setting before using them within a trial different from the original setting of validation (van de Steeg, Sielk, Pentzek, Bakx, & Altiner, 2009).

Adherence studies comparing self-report with prescription refill records

Some cross-sectional studies that were done to compare Morisky 4-item scale and a new 8-item scale (MMAS) and prescription refill records are illustrated in the Table 2.3.

Table 2.3: Adherence Studies Comparing Self-report with Prescription Refill Records

Guenette et. al. (2005)	Aim	To assess the level of agreement between a self-reported measure of adherence and pharmacy data.
	Setting and study population	• 17 pharmacists recruited 189 individuals aged 65 or above • In-home interview • All the prescribed drugs for last 4 months
	Adherence measure	• Morisky 4-item was administered • Continuous Single-Interval Medication Availability (CMA) • 80% cut-off value • Adherence by individual and adherence by drug • Agreement: kappa statistics
	Results	• Adherence rate by self-report: 48% • Adherence rate by pharmacy records: 50% • Level of agreement: slight (kappa=0.16[CI:0.02-0.30])
	Conclusion	There is a poor agreement between self-reported measure of adherence and adherence with pharmacy records

Table 2.3: Adherence Studies Comparing Self-report with prescription Refill Records

Wang et.al. (2004)	Aim	To compare self-report (Telephone Survey) and filled prescriptions to assess how well patients report noncompliance with anti-hypertensive medications
	Setting and Study population	• 200 antihypertensive patients aged 55 or above from a large HMO or VAMC • Monotherapy
	Adherence measure	• Telephone survey: 1) if you ever missed taking a dose • The frequency with which you missed taking a dose • Pharmacy refill records: No. and % of days covered by antihypertensive medications • Spearman correlation and kappa statistics
	Results	• Poor agreement between the two methods (0.15) • Very poor agreement between categorical measures (kappa = 0.12)
	Conclusion	• There is a poor agreement between self-reported measure of adherence and adherence with pharmacy records

Table 2.3: Adherence Studies Comparing Self-report with prescription Refill Records

Krousel-Wood and Morisky DE et. al (2009)		To evaluate the association and concordance of the new 8-item Morisky Medication Adherence Scale (MMAS) with pharmacy fill data
	Setting and study population	87 community-dwelling seniors with hypertension aged 65 or above, taking atleast one antihypertensive medication
	Adherence measures	• MMAS was administered [high adherence (score:8), medium adherence (score 6 to <8) and low adherence (score <6) • Adherence rate was calculated by MPR, CMA, and CMG • Pharmacy non-persistence: less than 0.8 for CSA and MPR • less than 0.2 for CMG Agreement: Log binomial regression model (% concordance)
	Results	• Overall 58%, 33%, and 9% of participants had high, medium and low medication adherence by MMAS • Concordance between MMAS and CSA, MPR & CMG was 75%
	Conclusion	MMAS is significantly associated with antihypertensive drug pharmacy refill adherence and further validation of the MMAS is required

The conclusion drawn from this literature review is that currently there is no "gold standard" measure of adherence. All these studies have been performed in various different settings and various different measures of adherence have been used. However, assessing medication-taking behavior still remains a challenge. These various adherence measures have yielded significant differences in estimates across different disease states, classes of medications, and patient populations. None of the studies have included very older adults (above the age of 90). Further research is imperative to explore the medication-taking behavior in the older adults.

This study will evaluate the agreement between three different measures of adherence in an older adult hypertensive population.

CHAPTER 3 METHODOLOGY

This chapter explains in detail the methodology that was used in this study. The first two sections of the chapter explain the aims of the study and the study design. In the section of study design, the settings in which the study was conducted, study population, participant recruitment, and data collection methods are described. The third section explains the instruments that were used to assess medication adherence in older adults and the final section depicts the analyses that were performed.

Aims of the study

The main objective of the study was to evaluate the agreement between Morisky Medication Adherence Scale (MMAS) and Brief Medication Questionnaire (BMQ) self-report methods and prescription refill records.

Specific Aim 1: Measure adherence to anti-hypertensive medications using MMAS in older adults.

Specific Aim 2: Measure adherence to anti-hypertensive medications using BMQ in older adults.

Specific Aim 3: Measure adherence to antihypertensive medications using prescription refill records in older adults.

Specific Aim 4: Evaluate the agreement between the adherence rate measured by MMAS and prescription refill records in older adults.

Specific Aim 5: Evaluate the agreement between the adherence rate measured by BMQ and prescription refill records in older adults.

Specific Aim 6: Evaluate the agreement between adherence rate measured by MMAS and BMQ in older adults.

Study Design

Setting

This was an observational cross-sectional study. The study was conducted in a large independent-living retirement community, Imperial Plaza, located in Richmond, Virginia. Imperial Plaza's community consists of about 850 independently-living residents. It is one of the largest retirement communities in the state for older adults. The average age of the residents is approximately 84 years. For the purpose of the current study this was a suitable setting to recruit older adults, including those above the age of 90 years. Imperial Plaza also has an on-site pharmacy, Plaza Professional Pharmacy, for their residents. Prescription fill records of the participants were obtained from this pharmacy. Furthermore, Plaza Professional Pharmacy serves as an experiential training site for pharmacy students who regularly work with residents in the community providing medication-related services and education.

The study protocol and consent form were developed in January 2009. This protocol and consent document was reviewed and approved by the Virginia Commonwealth University Institutional Review Board, Office of Human Subjects Protection in March 2009. This study was submitted as an expedited review. Participants provided informed consent to participate in the study; including consent to access their prescription records for their antihypertensive medications at Plaza Professional Pharmacy. Volunteers were provided with an incentive of $10 in "Plaza Dollars" to be spent for services at Imperial Plaza to participate in the study. This study was funded by the principal investigator of the study.

Study population

This study enrolled independently-living older adults residing at Imperial Plaza who filled their prescription for antihypertensive therapy at Plaza Professional Pharmacy.

Study inclusion criteria:

Volunteers were eligible for the study if they were:

1. Aged 65 years or older.
2. Able to read and converse in English.
3. Residing at Imperial Plaza for more than 6 months.
4. Diagnosed with hypertension.
5. Prescribed at least one antihypertensive medication filled at Plaza Professional Pharmacy.
6. In control of their own medication administration. Participants could be using a pill box to organize their medications.

Study exclusion criteria:

Volunteers were excluded from participating in the study if they were:

1. Receiving medications for the treatment of dementia. Potential volunteers were asked if they were currently taking any medications for cognitive impairment. If the volunteers answered "yes" to the above question they were excluded from the study. If the volunteers answered no, but were found to have medications for dementia in their prescription refill records, they were excluded.

2. Residents in assisted-living where medications are administered by facility staff.
3. Using mail delivery to receive any of their antihypertensive medications.
4. Unable to provide informed consent.

Participant recruitment

Several approaches were used to recruit volunteers to participate in this study. An advertising flyer and a brochure describing the study were prepared and approved by the VCU IRB. The study brochure included an overview of the questions they would be asked, study eligibility criteria, the purpose of the study and the incentive information. Participants were asked to participate if they were taking medications for 'high blood pressure'. Study flyers were posted on the doors to the pharmacy and were distributed to all residents in the monthly pharmacy newsletter. An announcement about the study was also included in several issues of the weekly director's newsletter in Imperial Plaza community. In addition, participants in Plaza Professional Pharmacy's weekly blood pressure monitoring program were invited to participate in the study as they waited in line to have their blood pressure measured. The blood pressure monitoring program is a free service available to all the residents at Imperial Plaza. Study advertisement flyers and study brochures were distributed among people who visited weekly blood pressure sessions. Recruitment brochures were also distributed by the pharmacists at Plaza Professional Pharmacy along with prescription refills for antihypertensive medications. Interested residents were provided with a copy of the IRB approved consent form and given the opportunity to ask questions about study participation. Residents were given

time to review the consent document with their family and/or health care provider before deciding to participate.

Data collection

Consent was obtained from the participants prior to their interview. The interview of each participant took place either in their apartment or the Pharmacy clinic located at Imperial Plaza, according to their convenience. The data was collected over a period of 3 months. Participants were recruited from April 2009 to July 2009. They were asked to gather all their blood-pressure lowering medications at the time of the interview. Interviews were taken with a fixed script for both self-report questionnaires. The overall time burden to complete data collection for each patient was 30-45 minutes.

The main objective of this study was to assess the agreement between self-report measure of adherence and adherence based on prescription records measure in older adults. This study was not powered for statistical tests of significance. The recruitment goal was to enroll a minimum of 50 patients from the independent-living community. Thirty-five residents volunteered to participate during the study time period. Three volunteers were excluded from the study. These volunteers did not have complete information (6 month refill history) on at least one of their anti-hypertensive medications in the prescription records. Thus 32 participants were interviewed and records of their prescription refills were obtained from the on-site pharmacy. Participants' prescription records for antihypertensive drugs were obtained for a period of 6 months starting from October 2008 to March 2009. The electronic records from the pharmacy included the

brand or generic name of the prescribed drug(s), the dose, the quantity, the dates the drug(s) were dispensed, and personal dosage instructions regarding the doses per day and the pills per dose.

Adherence Measures

Medication adherence was assessed using 3 previously validated methods: Morisky Medication Adherence Scale (MMAS) and Brief Medication Questionnaire (BMQ) and Prescription refill records. All these measures relate to commonly prescribed medications for hypertension such as diuretics, β-adrenergic receptor antagonists, α-receptor antagonists, angiotensin II receptor antagonists, angiotensin-converting enzyme inhibitors and calcium channel blockers. For patients prescribed just one of these agents, the adherence measure reflects just that drug. For patients prescribed 2 or more of these medications the adherence measure reflects the average adherence among these drugs.

Self –report methods

DiMatteo indicated that self reporting has been used in 25.5% of the studies that measured non-adherence (DiMatteo, 2004). Self-report is easy to use and is inexpensive, hence its one of the preferred methods in research as well as clinical practice. (MacLaughlin et al., 2005) In this study self-reported adherence was measured using the 8-item MMAS and BMQ (Morisky et al., 2008; Svarstad et al., 1999).

1) Morisky Medication Adherence Scale (MMAS)

Morisky et. al. developed a 4-item medication adherence scale in 1986 (Morisky et al., 1986). It has been widely used in the literature to measure adherence to medications for several chronic conditions (Morisky et al., 1986; Raehl et al., 2006; Rickles & Svarstad, 2007; Spiers & Kutzik, 1995; Stewart, 1987; van de Steeg et al., 2009). From the previously validated 4-item scale, a new 8-item MMAS was developed (Morisky et al., 2008). This new scale supplemented additional items to address the circumstances surrounding non-adherence behavior. Psychometric properties of this 8-item scale were determined in a randomized experimental pretest and protest study design. This was done over a 12-month period in 1367 patients who were diagnosed with hypertension and were attending an outpatient clinic of a large teaching hospital. A significant relationship between the adherence scale and blood pressure control was found (chi-square, 6.6; $p<0.05$).

Sensitivity and specificity of the 8- item scale were 93% and 53% respectively. Due to this scale's high sensitivity, it could be used to identify patients with low medication adherence and patients with uncontrolled blood pressure. The specificity indicates moderate performance of the scale in identifying patients who do not have problems with medication adherence and have their blood pressure under control relative to all those with controlled blood pressure (Krousel-Wood et al., 2009; Morisky et al., 2008). Significant correlation was found between the new 8-item scale and the previous 4-item scale (Morisky et al., 2008). The new scale has been determined to have higher reliability compared with the 4-item Morisky scale ($\alpha = 0.83$ vs. $\alpha = 0.61$).

The questions in this scale are phrased to avoid the "yes-saying" bias. Since there is a tendency for patients to give their physicians or other health care providers' positive answers, the wording of the questions in this scale motivates patients to report any difficulties that they may be facing in following their medication regimen. This is a simple and economical tool to use and can provide real-time feedback regarding adherence behavior and potential reasons for poor adherence including social, situational, and behavioral factors affecting adherence. MMAS has been trichomotized into 3 levels of adherence, in order to facilitate its use in clinical practice: high adherence (Score 8), medium adherence (score 6 to <8) and low adherence (score <6). The 8 questions asked during the interview are given in the Table 3.1.

Table 3.1: Item on Morisky 8-item scale (Morisky et al., 2008)

	No = 0	Yes = 1
1. Do you sometimes forget to take your [health concern] pills		
2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your [health concern] medicine?		
3. Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?		
4. When you travel or leave home, do you sometimes forget to bring along your [health concern] medication?		
5. Did you take your [health concern] medicine yesterday?		
6. When you feel like your [health concern] is under control, do you sometimes stop taking your medicine?		
7. Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your blood pressure treatment plan?		

8. How often do you have difficulty remembering to take all your medications?
Never = 0; Almost never = 1; Sometimes = 2; Quite often = 3; Always = 4

Before the interview began, participants were explained the purpose of MMAS questions. For this reason they were told that patients on blood pressure lowering medications have identified several issues regarding their medication-taking behavior and their experiences were of interests for the current study. They were also informed that there were no right or wrong answers and were asked to answer each question based on their personal experience with medications (Morisky et al., 2008).

Positive answers obtained for items 1-4, 6, 7, and 8 were coded as yes = 1 and for negative answers no = 0. Item 8 was divided by 4 to calculate a summated score. This procedure standardizes the 5-point Likert scale. The total score of the scale ranges from 0 to 8. Participants with the total score of 6-8 were deemed adherent and participants with the total score below 6 were deemed non-adherent for the purpose of this study.

2) Brief Medication Questionnaire (BMQ) (Svarstad et al., 1999)

Svarstad et. al. developed BMQ which involves a patient interview examining patient medication use using three subscales or screens: Regimen, Belief, and Recall. The fourth screen is called as access barrier which evaluates the potential reasons for medication non-adherence (Svarstad et al., 1999). The sensitivity and reliability of BMQ was evaluated using Medication Event Monitoring System (MEMS®) in patients who were prescribed enalopril and captopril (angiotensin-converting enzyme [ACE] inhibitors). MEMS records each time the cap is opened on the medication vial. Forty-eight participants were randomly assigned to two groups: one group received their enalopril and captopril in a MEMS container (n = 22) and the other group received a

standard vial (n = 22). MEMS were considered as a "gold-standard" of adherence measurement. BMQ was found to have 90% sensitivity and 80% specificity. The accuracy of BMQ was found to be 85%. This was the first tool which demonstrated that sensitivity levels vary by type of non-adherence and type of screening tool. Also, this tool was validated in a test population with multiple drugs and refill prescriptions, which are the factors known to reduce the sensitivity of self-report adherence measures (Stewart, 1987). Internal consistency as measured by Cronbach's alpha, during instrument developed ranged from 0.55 to 0.86 across diverse populations. (22) Since its development, the BMQ has been used widely in descriptive research on medication adherence, and has begun to emerge in intervention studies that involve patient education and other cognitive intervention components (Haynes et al., 2008).

A newer version of BMQ (2003) with some additional new items to assess financial barriers, and information on discontinued medication was obtained from the author. (Svarstad et al., 1999) Permission was obtained to implement the current version of BMQ in the current study.

The first screen includes 5 items that measure adherence behavior for the past week and is called the "*Regimen screen"* for potential non-adherence. Participants were asked to mention: Medication name and strength, number of days they took the pill, number of times per day and number of pills they took. They were also asked to mention if they missed taking any pill and if they said yes then they were asked to mention number of times they missed taking it. To understand how much a participant knows about his medication he was asked the reason why he was taking that particular pill.

If a participant reported "don't know" in response to all of the above questions he indicated a presence of non-adherence and was deemed nonadherent.

The *"Belief Screen"* measures two beliefs that have been linked to non-adherence in past studies. These particular items address patient concerns or doubts about the efficacy of a given medication and concerns about unwanted side effects, short-term or long-term risks, or other bothersome features of a given medication. Participants were asked how well the medicine works for them. The response were noted as 1 = very; 2 = somewhat; 3 = not at all and 4 = don't know. Participants were deemed "non-adherent" if they responded "not well" or "don't know" when asked how well the target medication works for them and if the medication was identified as bothersome. Item scores are summed to obtain a total belief score, with positive scores indicating one or more belief barriers (ranging from 0-2) (Svarstad et al., 1999).

The third screen is called the *"Recall Screen"* and includes two items that measure potential problems remembering all doses. Participants were deemed "adherent" if they had a single dose regimen (once daily) and reported that it is "not at all" hard to remember all the pills. Participants were deemed "non-adherent" if they had a multiple dose regimen (two or more times per day), or reported that it is "very" or "somewhat" hard to remember all the pills, and a score of "2" if both indicators are present (Svarstad et al., 1999).

The last *"access screen"* assessed any difficulties opening the container, reading labels, obtaining refills, and other practical issues participants were facing (Svarstad et al., 1999). If a participant reported any difficulty paying for medication and difficulty in

getting refills in time, participants was deemed to have poor access to the medications which is a potential barrier to medication adherence. (World Health Organization, 2003)

BMQ screens are shown in the Table 3.2.

Table 3.2: Brief Medication Questionnaire (Svarstad et al., 1999)

1. **Regimen Screen** (Past week)
   a. Medication name and strength
   b. How many days did you take it?
   c. How many times per day did you take it?
   d. How many pills did you take each time?
   e. How many times did you miss taking a pill?
   f. For what reasons were you taking it?
   g. How well does this medicine work for you?
      1 = very; 2 = somewhat; 3 = not at all; 4 = don't know
2. **Belief Screen**
   Do any of your medications bother you in any way?
   a. If 'yes', please name the medication and explain how it bothers you?
3. **Recall screen** (Past 6 months)
   Did you stop taking any Medications in the past 6 month?
   If 'yes', please tell: a. Medication name
   b. For what reason were you taking it
   c. How well did the medicine work for you?
      1 = very; 2 = somewhat; 3 = not at all and 4 = don't know
   d. How much did it bother you?
      0 = none; 1 = a little and 2 = a lot
   e. For what reason did you stop taking it?
4. **Access screen**
   a. My medication causes side effects
   b. It is hard to remember all the doses
   c. It is hard to pay for the medication
   d. It is hard to open the container
   e. It is hard to get my refill on time
   f. It is hard to read the print on the container
   g. The dosage times are inconvenient
   h. My medication causes other problems or concern
      If any other problem or concern, please explain:
      Response: 0 = None 1 = A little 2 = A lot

3) Prescription Refill records

Prescription refills record is a frequently used method to measure medication adherence objectively (Kripalani et al., 2007; Vik et al., 2004). With the advent of centralized computerized refill records, the use of pharmacy prescription refill has increased dramatically. Pharmacy records used to estimate non-adherence are often readily available and provide an "economical approach" in estimating adherence (Vik et al., 2004). More than 200 studies have assessed medication adherence using prescription records (Andrade, Kahler, Frech, & Chan, 2006). Prescription refill records are very useful in assessing medication adherence in population-based studies that need to assess drug exposure retrospectively. Refill compliance measures are also appropriate for pharmacy-based interventions to improve medication acquisition in clinical settings (Steiner & Prochazka, 1997).

For the purpose of the current study, adherence rate to antihypertensive medications in older adults was calculated by Medication Possession Ratio (MPR) using participants' prescription refill records for the past 6 months. Possession of medication is the required initial step for patients to actually consume the drugs and MPR helps identify long-gaps in treatment with antihypertensive medication that may lead to adverse outcomes. Calculating MPR is a well-accepted methodology to measure medication use in research with pharmacy refill records (Hess, Raebel, Conner, & Malone, 2006). MPR was defined as supply of medication in days divided by the total number of days between the first and the last refill date. The value obtained was multiplied by 100 to convert to a percentage. The numerator was the sum of all days supplied regardless of whether

prescriptions involved overlapping days. The number of days was counted beginning from the fill date of the patient's first fill pharmacy claim.

Days' supply of the last observed pharmacy claim was not included in the summation of the supply of medication as no antihypertensive pharmacy refill activity was observed after that refill date for the purpose of our study. Adherence was capped at 100% i.e. MPR values greater than 1 were reduced to 1. Calculations of MPR are demonstrated in the Table 3.3.

Table 3.3: MPR Calculation to Measure Adherence Rate Using Prescription Refill Records

Days' supply obtained	30	30	30	30	30	30
Date fill occurred	10/3/08	11/4/08	12/5/08	1/6/09	2/6/09	3/10/09
Interval (in days)		32	31	32	31	32

$$\text{MPR} = \frac{\text{Days' supply}}{\text{Interval of days}} = 150/158 = 0.9493 = 94.93\%$$

Drug-specific MPR's were calculated. For patients who were taking more than one antihypertensive medication, MPR were calculated for each medication and then averaged across all the medications to assign a single MPR to each participant. Patients were categorized as adherent if overall MPR value was 80% or above. Based on previous studies, 80% cut-off value was used to define adequate medication adherence using pharmacy refill data. (Sikka, Xia, & Aubert, 2005)

This cut-off was specified a priori and based on a study Psay et. al that indicated that patients who took less than 80% of their hypertensive medication were at a 4-fold risk for acute cardiac events than patients who took 80% or more of their medications. Participants with a MMAS score of 6 or above were deemed adherent, thus the adherence cut-off correlates well with the prescription refill records cut-off value.

Data Management and analyses

The main objective of this study was to evaluate the agreement between the self-report method of medication adherence and prescription fill records in the population taking blood pressure lowering medications. All study records were stored in a locked file cabinet in the investigator's office. All patient data was de-identified when entered into the study database in HIPAA compliant manner. The study database was password protected. Study data was entered into an electronic spreadsheet. All analyses were done using JMP® 8.

Descriptive statistics including the mean and standard deviation or median and 25th and 75th percentiles for continuous variable or proportion with 95% confidence intervals for categorical variables were calculated for all demographic and clinical characteristics measured. Demographic characteristics included age, gender, ethnicity, socioeconomic status, and co-morbid conditions. To evaluate participants' socioeconomic status they were asked if they had any difficulty paying for their medications in past 6 months. The response was categorized as yes or no. All the participants responded to this question saying no, they did not have any difficulty paying for their medications in past 6 months. Hence, the demographic variable socioeconomic status was not included in the analysis. Due to small sample size there was insufficient variability to calculate co-morbid conditions using ICD-9 codes thus, this demographic variable was not included in the analysis.

Clinical characteristics such as class of antihypertensive medications, number of antihypertensive drugs, and combination drug pill were included in the data analysis.

Overall adherence rates by MMAS, BMQ, and prescription refill records were analyzed using distribution statistics. Using the cut-off values and based on participants responses, they were dichotomized into two groups as adherent and non-adherent. Participants with the score of 6 to 8 were considered adherent and participants with the score below 6 were considered non-adherent. For BMQ participants were screened for non-adherence individually for all the four screens. For MPR the cut-off value of 80% was used to deem participants adherent and non-adherent.

Kappa (*k*) statistics was used to define the agreement between MMAS and prescription refill records, between BMQ and prescription refill records, and between MMAS and BMQ.

The strength of the agreement was assessed with a commonly used classification scale for kappa coefficients. Kappa values range from -1 and 1.
-1 to 0.00 = poor, 0.00 to 0.02 = slight, 0.21 – 0.40 = fair, 0.41 – 0.60 = moderate, 0.61 – 0.80 = substantial and 0.81 to 100 = almost perfect (Landis & Koch, 1977).

During the interview individual participants observations on how he/she manages medication, medication habits, concerns about the medications and any other useful information were recorded.

CHAPTER 3 RESULTS

Demographics characteristics

Overall 35 residents volunteered to participate in the study. Of these, 32 met the inclusion/exclusion criteria. The average age of the participants was 88 (SD = 5.5) years. The oldest participant was 97 years old and the youngest participant was 76 years old. There were 14 (43.8%) participants aged 90 and above and 18 (56.3%) participants who were aged 89 or below. Out of total of 32 participants, there were 21 (65.6%) women and 11 (34.4%) men in the study. There were 30 (93.7%) Caucasian participants whereas there were 2 (6.25%) African-American participants in the study. Thus very little ethnic diversity was present in the population. Participants' socioeconomic status was assessed by asking them, whether they had any difficulty paying for their medications in the past 6 months. It was found that all the participants had no difficulty in paying for their medications. Due to Medicare Part D they were more likely to be able to afford their medications than uninsured populations. Patients' demographic characteristics are shown in Table 4.

Table 4.1: Participant's Demographic Characteristics

Variables	N (%)
Age in years	
≤ 89	18(56.3%)
≥ 90	14(43.8%)
Gender	
Men	11(34.4%)
Women	21(65.6%)
Race	
Caucasian	30(93.8%)
African-American	2(6.3%)

Clinical characteristics

Overall 23 (71.9%) participants were taking diuretics. Diuretics are the first line therapy for isolated systolic hypertension according to treatment guidelines for blood pressure management (*The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC 7).*December 2003).

Only 7 (21.9%) participants were taking monotherapy for hypertension. Overall 17 (53.1%) participants were taking 2 antihypertensive medications, 7 (21.9%) participants were taking 3 antihypertensive medications. Only 1 (3.1%) participant was taking 4 antihypertensive medications.

Of the 32 participants 7 (21.9%) were taking just 1 pill and 12 (37.5%) participants were taking two pills and rest 13 (40.6%) participants were taking 3 or more number of pills per day.

Overall 20 (63%) of the participants were using pill boxes to manage their medications.

Overall 9 (28.1%) participants were taking a combination product of antihypertensive medications. The clinical characteristics of the patients are shown in Table 4.2.

Table 4.2: Participant's Clinical Characteristics

Variable	N (%)
No. of drugs	
1	4(12.5%)
2	20(62.5%)
3	7(21.9%)
4	1(3.1%)
No. of pills	
1	7(21.9%)
2	12(37.5%)
Combination pill	
Yes	9(28.1%)
No	23(71.8%)

The overall adherence rates measured by prescription refill records, MMAS, BMQ regimen, BMQ belief and BMQ recall screens were 84.4%, 59.4%, 68.8%, 93.4% and 59.4% respectively.

Out of 14 participants aged 90 or above, 11 participants (78.6%) were found to be adherent according to MPR and BMQ Regimen barrier. Ten participants (71.4%) were found to be adherent according MMAS and BMQ recall screen. All the older adults aged 90 and above had 100% adherence rate according to BMQ belief screen.

In contrast; out of 18 participants aged 89 or below, 16 participants (88.9%) were found adherent according to MPR and BMQ belief screen. Based on MMAS and BMQ

recall screen 9 (50%) of the participants were adherent to their antihypertensive medications. According to BMQ regimen screen, 11 participants (61.1%) were adherent.

Participants aged 90 and above were found to be more adherent to their antihypertensive medications according to MMAS and BMQ belief screen. The adherence rate in different age groups is shown in the Table 4.3.

Table 4.3: Adherence Rate Across Two Age Groups

Adherence measure	Adherence rate Participants aged ≥ 90 (n=14)	Adherence rate Participants aged ≤ 89 (n=18)
MPR	11 (78.6%)	16 (88.9%)
MMAS	10 (71.4%)	9 (50%)
BMQ regimen screen	11 (78.6%)	11 (61.1%)
BMQ belief screen	14 (100%)	16 (88.9%)
BMQ recall screen	10 (71.4%)	9 (50%)

Agreement between adherence measures

Very poor agreement between prescription refill records and self-report measures was observed. There was a slight agreement between MMAS and BMQ belief screen and substantial agreement between MMAS and BMQ regimen screen. Good agreement between MMAS and BMQ recall screen was observed.

Very poor agreement between prescription refill data and MMAS self-report (kappa = -0.004), prescription refill data and BMQ regimen screen (kappa = -0.095), prescription refill data and BMQ belief screen (kappa = -0.098) and between prescription fill data and BMQ recall screen (kappa = -0.004) was found.

Slight agreement between MMAS and BMQ belief screen was found (kappa = 0.18). However, substantial agreement between MMAS and BMQ regimen screen was observed (kappa = 0.80). There was a good agreement between MMAS and BMQ recall (kappa = 0.87). Agreement kappa values are shown in the Table 4.4.

Table 4.4: Agreement Statistics

Adherence measure	Kappa value	Strength of agreement
Prescription refill records & MMAS	-0.004	Poor
Prescription refill records & BMQ Regimen Screen	-0.095	Poor
Prescription refill records & BMQ Belief Screen	-0.098	Poor
Prescription refill records & BMQ Recall screen	-0.004	Poor
MMAS and BMQ Regimen screen	0.18	Slight
MMAS and BMQ Belief screen	0.80	Substantial
MMAS and BMQ Recall screen	0.87	Good

Qualitative observations

1) Residents of Imperial Plaza were somewhat hesitant to participate in the study. Some residents seem to believe that participation in research studies is harmful. They like to consult their physician or family before participating in the study. Some of the residents were not willing to participate because they had hearing impairment.
2) Most of the participants were very disciplined and organized with their medications. They stored them at a fixed place or in weekly pill boxes so that they could remember to take them all the time. Most of the participants were using weekly/daily pill boxes as an aid for them to be able to remember to take their medications. However, some residents would say that they had taken their medications even though pills were found in the pill boxes that should have been taken.
3) One of the resident had already participated in the study and she was found to be adherent with both self-report methods and prescription refill data. However, she had no recollection of participating in the study after a month and she showed interest in participating again. This observation questions the reliability of self-report questionnaires.
4) It was observed that participants aged above 90 years were less likely to report that they have missed taking their medications. They seemed to want to believe that with increasing age they still have good memory and were proud of this fact.

This belief was supported by the relatively higher rate of adherence found in them as compared to those aged below 90 years. Participants did mention that they sometime do not take their medications in the morning if they want drive or go out, as their antihypertensive medication makes them feel dizzy.

5) The study population had easy access to medications because only residents who were filling their prescription for antihypertensive medications at on-site Plaza Pharmacy were recruited in the study.
6) There was a positive atmosphere and a very encouraging patient-pharmacist relationship present in the community. It has been shown that the pharmacists in collaboration with physicians can play an active role in increasing medication adherence (Haskard Zolnierek & Dimatteo, 2009; McDonald et al., 2002; Mihalko et al., 2004; Sullivan). Pharmacists at Plaza Professional Pharmacy were very efficient in developing friendly relationships with their patients and communicating the benefits of the treatment to them. This information was gathered during BMQ access barrier, when participants were asked if they had any difficulty getting their refills on time.
7) Most of the participants were chronic users of antihypertensive medications and they did understand the benefits of the treatment. None of the participants were found to be at risk for non-adherence when screened with BMQ belief screen. Strong health beliefs are required to adhere to the treatment (Lau et al., 2008; Lowry et al., 2005).

From all the above observations it is clear that, there is no single reason for medication non-adherence thus there can be no "one size fits all" approach to improving adherence (World health organization, 2003).

CHAPTER 5 DISCUSSION

The main purpose of this study was to assess agreement between adherence as measured by two different self-report methods and prescription refill records in older adults taking medications for hypertension. Main finding and strengths of the study will be discussed in this chapter. This chapter will also address the study's limitations and future directions.

Main finding

Poor agreement was found between self-reported medication adherence and adherence measured using prescription refill record. When MMAS and the BMQ were compared with each other, substantial agreement was found. This indicated that both these methods address patients' adherence in a comparable way. Older adults aged above 90 years had greater rate of adherence with self-report questionnaires than participants aged below 90. This explains that patients with good adherence have better perception about their medications and stronger beliefs about the benefits of the medications.

Adherence measures

This is one of the few studies that evaluated agreement between three adherence methods by interviewing patients with the questionnaires, exclusively in older adults. Previous studies that have evaluated the agreement between self-report methods and prescription fill records have also found similar results as the current study (Cook et al., 2005; Wang et al., 2004).

Non-adherence in a population of older adult patients with congestive heart failure has been assessed using self-report method and similar results as the current study were found. The oldest elderly patient (>85 years old) had the highest adherence rate (Monane, Bohn, Gurwitz, Glynn, & Avorn, 1994). From the analysis of the current study it was found that older adults aged above 90 had higher rate of self-reported adherence than those aged below 90.

Recently one study validated MMAS 8-item scale and Medication Adherence Report Scale (MARS-5) for the measurement of adherence of 128 patients treated with antihypertensive drugs in primary care in Germany. Prescription refill records were used as a reference standard to compare these two self-report methods. The two questionnaires overestimated patients' adherence and turned out to be invalid for the setting they were used. However, reasonable specificity (72.8%) was found for MMAS (van de Steeg et al., 2009). However, the study did not include older adults specifically.

Thus the current study results are consistent and in agreement with other studies showing that the adherence as measured by self-report does not agree with the adherence measured using pharmacy records.

The discrepancies between the self-report method and prescription fill records adherence rate may be explained in different ways. First, these methods measure different concepts of adherence. MMAS recognizes patient's intentional and unintentional nonadherence whereas BMQ addresses the specifics of the therapeutic regimen, patient's beliefs about a particular regimen, and assess patient's access to the medications. Prescription refill records indirectly measure adherence by examining the length of time and quantity of medication acquired by the patient. Thus this method provides only a rough average of overall medication-taking behavior. It documents a patient's actions rather than a patient's intention.

Another explanation for the poor agreement is that self-reported measures evaluate adherence rate over different time frames. BMQ itself evaluated patient's medication-taking behavior over a period of a week, two weeks, and 6 months. Prescription fill data measured patients' medication taking behavior for the longest period of time. Participants 6 month's prescription refill records were analyzed to calculate their adherence rate. Good agreement between MMAS and BMQ can be explained by the similar structural formats of the two measures.

Even though patients' self-report is the easiest and most common method to measure adherence, it involves a risk of social desirability bias which may lead to overestimation of adherence (Raehl et al., 2006). It was observed in this study that older adults aged above 90 tend to give positive answers. Perhaps they have a tendency to want to show that, in spite of their old age, their memory is still good. They may do so with the intention to want to maintain their independent-living status. With the intention of

minimizing the social desirability bias in the study, participants were informed that information collected from their interviews would remain confidential. Most of the participants were interviewed at their homes to provide them with a more comfortable and familiar environment. The assumption behind this was that, this surrounding and detail information on the study will help them to be more honest and open about their medication-taking behavior and concerns. For example, one study pointed out that in a general practitioner's office patients may not be very willing to reveal their medication taking habits (van de Steeg et al., 2009). Practitioners may also be biased towards enrolling only adherent patient in studies (Spiers & Kutzik, 1995; van de Steeg et al., 2009). The interviewer of this study was not aware of participants' medication-taking habits at all, potentially reducing this type of bias in this study.

In this study, 63% of the participants were using weekly or daily pill boxes which are either filled by the participant, a family member or the pharmacist at Plaza Professional Pharmacy. In such a situation, when positive response for self-report questionnaires was obtained, the interviewer asked the participant to show the weekly pill containers. Some people did not take their weekly dose of the therapies evidenced by pills remaining in the pill box on days that should be empty, but reported that they did so. This may indicate that self-reported adherence is not always an accurate measure for older adults (Vik et al., 2004).

BMQ examines the patient's intentions and knowledge with respect to their medications. It was observed that some of the patients adhered to their therapy simply because physician instructed them to do so without understanding the purpose or goals of

therapy. On the other hand some patients do understand all the benefits of a give therapy, yet either choose not to adhere to avoid adverse drug reactions or they do not trust their prescribers (Guenette, Moisan, Preville, & Boyer, 2005). Considering the population of this study, most of the patients aged above 90 seemed concerned about their health and were disciplined with their medication-taking behavior. This may result in them having better health and quality of life than those who do not adhere to their therapy.

Pharmacy refill records also have some limitations. This method provides only a rough average of overall medication-taking behavior and documents patient's action rather than a patient's intention (A. Christensen, Osterberg, & Hansen, 2009; D. B. Christensen et al., 1997). It may underestimate the adherence rate if there is missing data on the prescription. For example, the mediations may be supplied by a different pharmacy for a period of time. However, this limitation did not impinge on the results of this study, as only the participants who refilled their prescriptions at the on-site Plaza Pharmacy were enrolled in the study. During hospitalization, medications are provided by the hospital and would appear as a gap in refill history. The refill history indicates nonadherence in this case, when the resident was actually adherent (Claesson, Morrison, Wertheimer, & Berger, 1999).

The cut-off value of 80% for adherence as assessed by prescription refill history was chosen based on past literature. Psay et. al performed a study that indicated that patients who took less than 80% of their hypertensive medication were at a 4-fold risk for acute cardiac events than patients who took 80% or more of their medications (Bramley, Gerbino, Nightengale, & Frech-Tamas, 2006; Psaty, Koepsell, Wagner, LoGerfo, & Inui,

1990). However, there is a need to clinically evaluate the level of medication adherence that distinguishes clinically significant adherence versus non-adherence (Karve et al., 2009). Longitudinal studies that measure medication adherence using a combination of subjective and objective method are required to determine the unambiguous cut-point above which there is a positive relationship between level of medication adherence and significant clinical outcomes for hypertensive patients (Wu et al., 2009; Wu et al., 2009). The adherence rate should be analyzed as a continuous measure instead of dichotomizing it using the 80% cut-off value for MPR values (Wu et al., 2008).

Issues related to difficulty accessing medication could not be evaluated in this study. Residents of one of the largest independent-living communities in Virginia participated in this study. This population has a relatively high socioeconomic status and participants indicated no difficulty paying for their medications. This population is eligible for Medicare Part D, which makes it more likely that they will have prescription drug coverage. This population had higher rates of adherence due to lesser issues with accessing their prescription drugs as they do not have transportation issues impairing their ability to get their medications. Previous studies have shown that African-Americans have poor medication adherence compared to Caucasian population (Cooper, 2009; Rizzo & Simons, 1997). The possible explanations for non-adherence were found to be low literacy levels and poor socioeconomic status among African-Americans (Cooper, 2009). As the study population was predominantly Caucasian, this may have also contributed to relatively high adherence rates in the study.

Wang. et. al. conducted a telephone survey on 200 hypertensive patients treated with a single anti-hypertensive agent in a large HMO to obtain self-reports of the frequency of missing antihypertensive therapy (Wang et al., 2004). In a population of older adults, particularly in those aged above 90 this method of a telephone survey may not be feasible due to communication difficulties for some older adults due to age-related hearing impairment. It is more challenging to interview older adults over the phone or through internet based services in order to understand their medication-taking behavior. Interviewing older adults with the self-report questionnaires is an ideal way to collect information on their medication-taking habits and to understand if they have any concerns with the treatment.

However, it was challenging to enroll older adults, especially older adults aged above 90 in this study as they were quite hesitant to participate. Some had the notion that they are put at risk during research studies and it is not necessary for them to participate. Some of the participants consulted their physicians or family before participating in the study. It was definitely very difficult to communicate the study purpose to these older adults. Some of the residents from independent-living facility called the interviewer to volunteer to participate and when they were contacted back to schedule an appointment they had no memory of volunteering to participate in the study. This suggests that even though these residents were living in an independent-living facility they might have been suffering from mild cognitive impairment.

The study was designed to compare three different adherence measures. Neither the self-report method nor the pharmacy-based adherence measure was considered to be the

gold standard for the purpose of this study. Unlike much of the prior literature in this area, this study focused exclusively on older adults and the average age was 88 years. It is still not clear that, whether chronic users have better adherence rates than those who newly being the therapy (Mallion, Baguet, Siche, Tremel, & de Gaudemaris, 1998; Mihalko et al., 2004). However, all the participants were chronic users of the antihypertensive medications, as found from their prescription refill history. This may have prevented confounding from the differences in medication adherence found between those who are just beginning a new medication regimen and those who have been following the regimen for a long time.

Overall this study contributes significantly to understanding if the self-report methods and prescription refill records are in agreement and also in evaluating older adults' medication-taking behavior qualitatively.

Limitations

The main limitation of this study was the small sample size. Less variability in the sample size prevented formal analysis of the predictors of adherence such as increasing age, polyphrmacy, and co-morbid conditions in older adults. It would have been interesting to see how these predictors affect the adherence rate among older adults aged above 90 since there have been varying results on these predictors in the past literature. This study was limited to older community-dwelling adults with managed care insurance and may not be representative of patients from other socioeconomic backgrounds.

Imperial Plaza's independent-living retirement community provides its residents with readily accessible pharmacy system and services. The weekly blood pressure monitoring program at Plaza pharmacy helps create awareness for benefits of the hypertension drug therapy among the residents. The results of the study are biased towards good adherence, because these facilities, education, and knowledge may have helped participants of the study to have positive attitude towards their antihypertensive treatment. The study population had very little racial, ethnic, and cultural diversity. According to Virginia department of aging, Virginia's older population is growing more racially and ethnically diverse, reflecting the growing racial and cultural diversity of the Commonwealth and the nation (*Virginia department for the aging.*)

The methods used to measure adherence rates in the study have some shortcomings too. The possibility of patients being affected by social desirability bias during interviews cannot be rejected. Different time frames of the self-report questionnaires and prescription

refill records may have lead to the disagreement between the measured adherence rates. MPR 80% cut-off value to identify adherent and non-adherent patients is not based on empirical data.

Future Directions

Further research should be directed in refining the results obtained from this study. There is a need to carry out similar studies in more ethnically and culturally diverse larger patient populations. A multi-center study would add to the generalizability of the study results. The issue of understanding different predictors of adherence especially in older adults aged above 90 could perhaps be addressed in future studies by including a more diverse patient population. For example, a self report method that may work well for a middle aged population may not be the most preferred approach in the older population. Thus from the available self report tools, we may need to determine which one would be the best to use in the older population.

There is a need to have a well-defined, valid, reliable, cost-effective tool that is accepted by both health care providers and patients to measure medication adherence. Widespread use of such a tool, which could provide insight into modifiable factors regarding adherence in different patient populations would lead to better understanding of nonadherence and lay the groundwork for interventions aimed at increasing adherence to therapies (McDonald et al., 2002). Adherence needs to be measured as a continuous variable, rather than categorizing it as adherent or non-adherent behavior, to ensure that all variations in treatment behavior are adequately captured (Mihalko et al., 2004).

To advance the research in this area it will be necessary to understand the medication-taking behavior of older adults with mild cognitive impairment in more depth as well.

Conclusions

The study was aimed at evaluating the agreement between self-report method and prescription refill records to measure antihypertensive medication adherence in older adults. Poor agreement between both self-report methods and prescription refill records was found. Substantial agreement was found between MMAS and BMQ, suggesting that both these self-report methods measure adherence in a comparable manner. Adherence rate was found to be greater in the study participants who understood the benefits of the treatment than those who did not understood them, which was observed with BMQ belief screen. Participants aged above 90 reported relatively higher rates of adherence with self-report than participants aged below 90. Composite measurement strategies that incorporate multiple types of measures are needed to assess adherence accurately.

Selection of a useful and reliable adherence measure in pharmacy practice is required, to screen for older adults who are non-adherent to their antihypertensive treatment and to evaluate outcomes of interventions to improve adherence. These findings suggest that further validation of these measures to assess medication adherence in older adults is required.

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APPENDIX A CONSENT FORM

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Measurement of Adherence to Anti-hypertensive Medications in Older Adults Using Self-report Compared to Prescription Fill records.

VCU IRB NO.: HM12071

SPONSOR: N/A

This consent form may contain words that you do not understand. Please ask the study staff to explain any words that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

PURPOSE OF THE STUDY

The purpose of this research study is to compare three different methods of determining whether older adults with high blood pressure are taking their medications as prescribed. You are being asked to participate in this study because you are over the age of 65, are taking at least one medication for high blood pressure, and have your prescriptions filled at Plaza Professional Pharmacy.

DESCRIPTION OF THE STUDY

If you decide to be in this research study, you will be asked to sign this consent form. In this study you will be complete two questionnaires about your use of medication for high blood pressure and may be asked additional questions about your medications for high blood pressure. With your consent, your prescription records during the last 6 months at Plaza Professional Pharmacy will also be reviewed. Participating in the study will take approximately one hour. No personal information about you will be revealed to staff or residents of Imperial Plaza during or after the study. Participants in the study will receive $10 in "Plaza Dollars" that can be spent for services at Imperial Plaza. Any new information that becomes available during the course of this research study which may relate to your willingness to continue participation will be provided to you.

BENEFITS TO YOU AND OTHERS

There is no direct benefit to you if you join this study. Participating in this study may benefit other individuals in the future to better manage their medications for high blood pressure and be adherent to them. This is not a treatment study. There is no guarantee that you will receive any medical benefits from being in this study.

COSTS

There are no costs for participating in this study other than the time you will spend in the sessions.

PAYMENT FOR PARTICIPATION

There is no compensation, but you will be offered an incentive of $10 in "Plaza Dollars" that can be spent for services at Imperial Plaza.

CONFIDENTIALITY

Information about you is being collected for research purposes only. All personal identifying information will be kept in password protected files, and these files will be deleted or destroyed upon completion of the study. Access to all data will be limited to study personnel.

Results of this study may be presented at meetings and published in scientific journals, but your name will not be used in these presentations or papers.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

You do not have to participate in this study. If you choose to participate, you may stop at any time without any penalty.

Your participation in this study may be stopped at any time by the study staff if you have not followed the instructions or the study staff thinks it is necessary for your health or safety.

QUESTIONS

In the future, you may have questions about your participation in this study. If you have any questions, complaints, or concerns about the research, contact:

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Associate Professor and Geriatric Specialist
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Priyanka Kakad, B. Pharm, MS student.
VCU School of Pharmacy
804-402-9352

If you have any questions about your rights as a participant in this study, you may contact:

Office for Research
Virginia Commonwealth University
800 East Leigh Street, Suite 113
P.O. Box 980568
Richmond, VA 23298
Telephone: 804-827-2157

You may also contact this number for general questions, concerns, or complaints about the research. Please call this number if you cannot reach the research team or wish to talk to someone else. Additional information about participation in research studies can be found at http://www.research.vcu.edu/irb/volunteers.htm.

CONSENT

I have been provided with an opportunity to read this consent form carefully. All of the questions that I wish to raise concerning this study have been answered.

By signing this consent form, I have not waived any of the legal rights or benefits, to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form once I have agreed to participate.

Participant name printed | Participant signature | Date

BVT / SH / 3/18/09
APPROVED

APPENDIX B STUDY ADVERTISEMENT

BVT / SH / 3/18/09
APPROVED

ATTENTION!!
DO YOU HAVE HIGH BLOOD PRESSURE?

Virginia Commonwealth University School of Pharmacy is conducting a study of older adults taking medications for high blood pressure who manage their own medications

The purpose of the study is to compare several different ways of measuring how patients take their medications

Participants will spend approximately one hour being interviewed by the researcher and completing two brief questionnaires

If you are aged 65 and above and if you fill your prescription for your blood pressure lowering medications at Plaza Professional Pharmacy please contact

Dr. Patricia Slattum, PharmD, PhD,
School of Pharmacy Virginia Commonwealth University
804-828-6355
pwslattu@vcu.edu

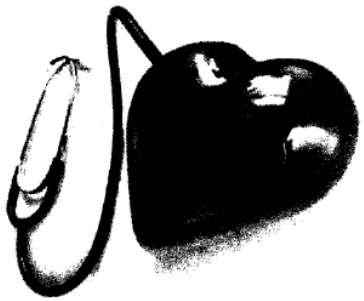
Participants will receive $10 in "Plaza Dollars"!!

2-16-2009

APPENDIX 1: Commonly used antihypertensive medications

APPENDIX C STUDY ADVERTISEMENT BROSHURE

The purpose of this study is to compare several different ways of measuring how patients take their medications.



Virginia Commonwealth University
VCU Medical Center

Blood Pressure Study

Do you take medications for your blood pressure?

Volunteers Needed!

You will receive 10 Plaza Dollars!!!

Please Contact:

Dr. Patricia Slattum
804-828-6355

410 N. 12th Street
Box 980533
Richmond
VA 23298-0533

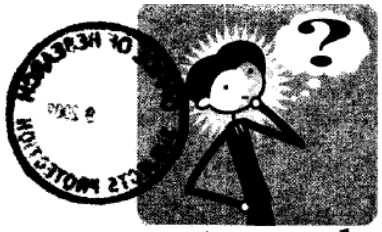
BJT/SH 6/9/09
APPROVED

This Study has been approved by the VCU Institutional Review Board.

You can participate if you are:

* Aged 65 and above
* Manage your own medications
* Fill your prescription for your blood pressure lowering medications at Plaza Professional Pharmacy

BJT / SH / 6/9/09
APPROVED



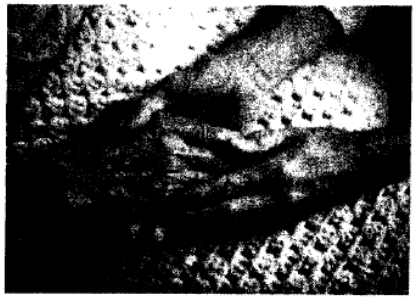
What do you have to do?

* Participate in a one-time interview to answer 10-15 questions about how you take your blood pressure medications
* The interview will not take longer than 1 hour
* Interview can be scheduled at your home or at the Pharmacy Clinic in Azalea 605 at a time convenient for you

Information about you is being collected for research purposes only.

Access to all data will be limited to study personnel .

No change in your medications will be made as part of this study



APPENDIX D ANTIHYPERTENISVE DRUGS

Oral Antihypertensives: Single drugs

Medication Class	Generic Name (Brand name)
Thiazide diuretics	Hydrochlorothiazide (Microzide, HydroDIURIL)
	Chlorothiazide (Diuril)
	Chlorthalidone
	Polythiazide (Renese)
	Indapamide (Lozol)
	Metolazone (Mykrox)
	Metolazone (Zaroxolyn)
Loop diuretics	Bumetanide (Bumex)
	Furosemide (Lasix)
	Torsemide (Demadex)
Potassium-sparing diuretics	Amiloride (Midamor)
	Triamterene (Dyrenium)
Aldosterone receptor blockers	Eplerenone (Inspra)
	Spironolactone (Aldactone)
Beta blockers	Atenolol (Tenormin)
	Betaxolol (Kerlone)
	Bisoprolol (Zebeta)
	Metoprolol (Lopressor)
	Metoprolol extended release (Toprol XL)
	Nadolol (Corgard)
	Propranolol (Inderal)
	Propranolol long-acting (Inderal LA)
	Timolol (Blocadren)
Beta blockers with intrinsic sympathomimetic activity	Acebutolol (Sectral)
	Penbutolol (Levatol)
	Pindolol (generic)
Combined α-blockers and beta blockers	Carvedilol (Coreg)
	Labetalol (Normodyne, Trandate)
Angiotensin-converting enzyme (ACE) inhibitors	Benazepril (Lotensin)
	Captopril (Capoten)
	Enalapril (Vasotec)
	Fosinopril (Monopril)
	Lisinopril (Prinivil, Zestril)
	Moexipril (Univasc)
	Perindopril (Aceon)
	Quinapril (Accupril)
	Ramipril (Altace)
	Trandolapril (Mavik)
Angiotensin II antagonists	Candesartan (Atacand)
	Eprosartan (Teveten)

	Irbesartan (Avapro)
	Losartan (Cozaar)
	Olmesartan (Benicar)
	Telmisartan (Micardis)
	Valsartan (Diovan)
Calcium channel blockers—Nondihydropyridines	Diltiazem extended release (Cardizem CD, Dilacor XR, Tiazac)
	Diltiazem extended release (Cardizem LA)
	Verapamil immediate release (Calan, Isoptin)
	Verapamil long acting (Calan SR, Isoptin SR)
	Verapamil (Coer, Covera HS, Verelan PM)
Calcium channel blockers—Dihydropyridines	Amlodipine (Norvasc)
	Felodipine (Plendil)
	Isradipine (Dynacirc CR)
	Nicardipine sustained release (Cardene SR)
	Nifedipine long-acting (Adalat CC, Procardia XL)
	Nisoldipine (Sular)
α_1 blockers	Doxazosin (Cardura)
	Prazosin (Minipress)
	Terazosin (Hytrin)
Central α_2 agonists and other centrally acting drugs	Clonidine (Catapres)
	Clonidine patch (Catapres-TTS)
	Methyldopa (Aldomet)
	Reserpine (generic)
	Guanfacine (Tenex)
Direct vasodilators	Hydralazine (Apresoline)
	Minoxidil (Loniten)

Oral Antihypertensives: Combination Drugs

Combination Type	Trade Name
ACE inhibitors and calcium channel blockers	Amlodipine-benazepril hydrochloride (Lotrel)
	Enalapril-felodipine (Lexxel)
	Trandolapril-verapamil (Tarka)
ACE inhibitors and diuretics	Benazepril-hydrochlorothiazide (Lotensin HCT)
	Captopril-hydrochlorothiazide (Capozide)
	Enalapril-hydrochlorothiazide (Vaseretic)
	Fosinopril-hydrochlorothiazide (Monopril/HCT)
	Lisinopril-hydrochlorothiazide (Prinzide, Zestoretic)
	Moexipril-hydrochlorothiazide (Uniretic)
	Quinapril-hydrochlorothiazide (Accuretic)
Angiotensin receptor blockers and diuretics	Candesartan-hydrochlorothiazide (Atacand HCT)
	Eprosartan-hydrochlorothiazide (Teveten-HCT)
	Irbesartan-hydrochlorothiazide (Avalide)
	Losartan-hydrochlorothiazide (Hyzaar)
	Olmesartan medoxomil-hydrochlorothiazide (Benicar

	HCT)
	Telmisartan-hydrochlorothiazide (Micardis-HCT)
	Valsartan-hydrochlorothiazide (Diovan-HCT)
Beta blockers and diuretics	Atenolol-chlorthalidone (Tenoretic)
	Bisoprolol-hydrochlorothiazide (Ziac)
	Metoprolol-hydrochlorothiazide (Lopressor HCT)
	Nadolol-bendroflumethiazide (Corzide)
	Propranolol LA-hydrochlorothiazide (Inderide LA)
	Timolol-hydrochlorothiazide (Timolide)
Centrally acting drug and diuretic	Methyldopa-hydrochlorothiazide (Aldoril)
	Reserpine-chlorthalidone (Demi-Regroton, Regroton)
	Reserpine-chlorothiazide (Diupres)
	Reserpine-hydrochlorothiazide (Hydropres)
Diuretic and diuretic	Amiloride-hydrochlorothiazide (Moduretic)
	Spironolactone-hydrochlorothiazide (Aldactazide)
	Triamterene-hydrochlorothiazide (Dyazide, Maxzide)

VITA

Education

August 2007 - Present	Virginia Commonwealth University, School of Pharmacy, Richmond, VA Masters of Science, Geriatric Pharmacotherapy candidate, to be awarded in August 2009
October 2003 - May 2007	University Institute of Chemical Technology, Mumbai, India Bachelor's of Pharmaceutical Sciences (B. Pharm. Sci.)
June 2001- June 2003	Saraswathi Education Society, Mumbai, India Higher Secondary Education (HSC)

Industrial Work Experience

June 2006 – July 2006	Pfizer Ltd, Mumbai, India Student intern
June 2005 – July 2005	Navketan Pharma Pvt. Ltd, Aurangabad, India Industrial trainee