A BEHAVIORAL FEEDBACK-BASED INTERVENTION TO IMPROVE MEDICATION ADHERENCE IN OLDER ADULTS WITH HYPERTENSION

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By

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The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled

A BEHAVIORAL FEEDBACK-BASED INTERVENTION TO IMPROVE MEDICATION ADHERENCE IN OLDER ADULTS WITH HYPERTENSION

Presented by Todd M. Ruppar

A candidate for the degree of Doctor of Philosophy

And hereby certify that, in their opinion, it is worthy of acceptance.

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Professor David Oliver

DEDICATION

I would like to thank my family, who endured years of trips to Columbia and countless days and nights of sequestering myself with my computer. I would also like to thank my parents, who provided invaluable help and encouragement. Without their support none of this would have been possible.

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Portions of Chapter 2 have been previously published in *Research and Theory for Nursing Practice*.

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ABSTRACT

Medication adherence among older adults is far below the levels needed for clinical effectiveness from many medications. Control of hypertension prevents the development of further chronic disease and limits morbidity and mortality. This exploratory RCT tests an 8-week behavioral feedback-based intervention to improve medication adherence and blood pressure control among older adults with hypertension. Fifteen adults aged 60 years and older were randomized to intervention or control groups. At 12 weeks post-randomization, outcomes were improved in the intervention group versus control group for medication adherence (Cohen's $d = 1.35$), systolic blood pressure ($d = 0.99$), and diastolic blood pressure ($d = 1.12$). The intervention was well-received by study participants, and outcomes show promise for improving adherence and blood pressure outcomes.

CHAPTER ONE: BACKGROUND OF THE PROBLEM

Introduction

Older adults are the fastest-growing age group in the United States today. As of the 2000 census, the number of people aged 65 years and older was estimated at approximately 35 million (He, Sengupta, Velkoff, & DeBarros, 2005). By 2030, this age group is expected to have more than doubled from its 2000 census level to approximately 72 million, making up 20% of the U.S. population (He et al., 2005).

Chronic Illness Self-Management in Older Adults: Antihypertensive Medication Adherence

Chronic illness has been defined as an irreversible health condition that can be expected to require ongoing supervision, observation, or care and affects a person's physical, psychological, and social functioning (Nodhturft et al., 2000; Tanner, 2004). Chronic illnesses are more common in older adults and are the cause of most of the leading causes of death and disability among the elderly (Anderson & Smith, 2005; Federal Interagency Forum on Aging-Related Statistics, 2004). Management of chronic illnesses is also more complex in older adults due in part to the frequent presence of comorbidities and to the physiologic changes that occur as a part of normal aging. Recent literature has noted the limitations of conventional medicine in treating and managing progressive chronic illnesses (Buckwalter et al., 2001; Marks, Allegrante, & Lorig, 2005). While new technologies to treat chronic conditions are promising, nearly all still require some form of health behavior change to achieve success, particularly for long-term illnesses with the potential for serious sequelae (Marks et al., 2005). Unfortunately,

most health care providers lack the training and tools to successfully intervene to change their patients' health behavior. Effective, practical interventions for health behavior are needed in clinical practice.

Hypertension is an especially common chronic illness. Hypertension is present in 26.7% of the U.S. adult population between ages 20 to 74 (National Center for Health Statistics, 2006). The prevalence increases with age. Sixty-seven percent of adults aged 60 years or older have hypertension, a rise from 58% just ten years earlier (Ostchega, Dillon, Hughes, Carroll, & Yoon, 2007). Uncontrolled hypertension increases the risk for heart attack, stroke, congestive heart failure, and kidney disease (Chobanian, Bakris, Black, Cushman, Green, Izzo, Jones, Materson, Oparil, Wright, Roccella et al., 2003; Stamler, Stamler, & Neaton, 1993; Vasan et al., 2001). Maintaining a normal blood pressure has been shown to be associated with a greater probability of living to age 85, and of living to age 85 without major health concerns (Terry et al., 2005). The most common treatment for managing hypertension involves the use of antihypertensive medications. These medications have been shown to effectively lower blood pressure (BP) and prevent the development of serious sequelae (Chobanian, Bakris, Black, Cushman, Green, Izzo, Jones, Materson, Oparil, Wright, Roccella et al., 2003). Unfortunately, failure to adhere to antihypertensive medication regimens can impede the effectiveness of therapy.

The World Health Organization defines adherence as "The extent to which a person's behaviour (taking medications, following a recommended diet and/or executing life-style changes) corresponds with the agreed recommendations of a health care provider" (Sabate, 2003, p. 13). Studies have reported levels of medication adherence

among the elderly ranging from 26% to 59% (Botelho & Dudrak, 1992; van Eijken, Tsang, Wensing, de Smet, & Grol, 2003). Adherence to a medication regimen requires a set of behaviors that include obtaining the medication; timely administration of the correct drug, dose, and route; and persisting with taking the medication as long as the medication is needed. Success at these behaviors can be hampered by many of the changes often seen with age. Sensory loss, disturbances in memory and cognition, depression, and lifestyle changes such as retirement can disrupt routines or affect skills previously used to maintain medication adherence (Brown et al., 2005; Conn, Taylor, & Miller, 1994; Coons et al., 1994; Gehi, Haas, Pipkin, & Whooley, 2005; Schlenk, Dunbar-Jacob, & Engberg, 2004; Vik, Maxwell, & Hogan, 2004). Effective interventions are needed to equip health care providers with tools to improve antihypertensive medication regimen adherence among their older patients. Many interventions have been tested to improve medication adherence in hypertension, but few addressing the unique needs of older adults. Of those that have been tested, there has been great variation in outcomes and ability to translate interventions into clinical practice.

Purpose

The primary aim of this exploratory study was to test whether a feedback-based adherence intervention improved medication adherence for community-dwelling older adults with hypertension. A secondary aim was to evaluate whether the intervention had any effect on resting blood pressure levels. The study achieved these aims by answering the following research questions:

Research Question 1: Were medication adherence rates in older adults with hypertension who received a feedback-based medication adherence intervention higher than those who received no intervention?

Research Question 2: Was resting blood pressure among older adults with hypertension who received a feedback-based medication adherence intervention lower than those who received no intervention?

The study also aimed to collect feasibility data on the intervention and study protocol by answering the following research questions:

Research Question 3: How many participants were necessary to recruit and assess to identify 15 older adults with <85% adherence?

Research Question 4: How much time did the intervention visits require?

Research Question 5: Did study participants report any problems or unexpected burden from study participation?

Significance to Nursing

Nurses are increasingly likely to be responsible for addressing medication adherence concerns with their patients. In most health care systems, nurses are the primary patient educators, administrators of patient medications during hospitalization, discharge planners, and case managers addressing medication concerns. Public health, community health, and parish nurses also frequently consult with patients and families regarding medication-taking behavior. Health care research has not conclusively identified a medication adherence intervention plan that is effective for all patients. Effective nurse-delivered medication adherence interventions are needed that address individual patients' health, functional status, medication regimen, medication-taking

skills, knowledge, resources, and beliefs, including cultural norms and expectations about health and pharmaceutical treatment.

CHAPTER TWO: REVIEW OF LITERATURE & THEORETICAL FRAMEWORK

Many studies have examined medication adherence interventions, but relatively few focus on older adult populations. This review of literature will first examine studies to improve antihypertensive medication adherence in older adults. Next, randomized controlled trials of medication adherence in older adults for any health condition will be reviewed. Finally, a conceptual framework which reflects the best available evidence will be proposed.

Medication Adherence Intervention Trials for Older Adults With Hypertension

Search Methods

Computerized database searches of English-language articles were conducted in MEDLINE (1950-2007), CINAHL (1982-2007), PsycINFO (1967-2007), Healthstar (1966-2007), the Cochrane Library (3rd Quarter 2007), and PubMed. Search terms used included *hypertension, medication adherence, medication compliance, medication concordance, patient compliance, patient adherence, drug counseling, medication counseling, medication education, pharmacist counseling, pharmacist consultation, prescribed regimen, self-medication,* and *pharmaceutical care*. Each of these terms was further limited with the keywords *aged* or *aged, 80 and over* and *intervention* or *intervention studies*. The retrieved citations' abstracts were reviewed for relevance. Eligible articles were required to be reports of intervention studies of persons with hypertension, have a mean age (for the intervention group) of 60 years or greater, and have a medication adherence outcome measure. When an article did not report outcomes, attempts were made to identify other reports of the same study with outcomes.

Description of Studies

Twenty study reports were determined to be eligible for review (see Figure 1). Articles were published between 1986 and 2006. The studies enrolled sample sizes from 16 to 7,274 participants. The total enrolled sample size for all reviewed studies was 10,550 participants. Most studies were conducted in the United States (n=12), with the remainder in Europe (n=6), Brazil (n=1), and Canada (n=1). Summary data of the reviewed studies is reported in Table 1.

Figure 1: *Study Inclusion Flowchart*

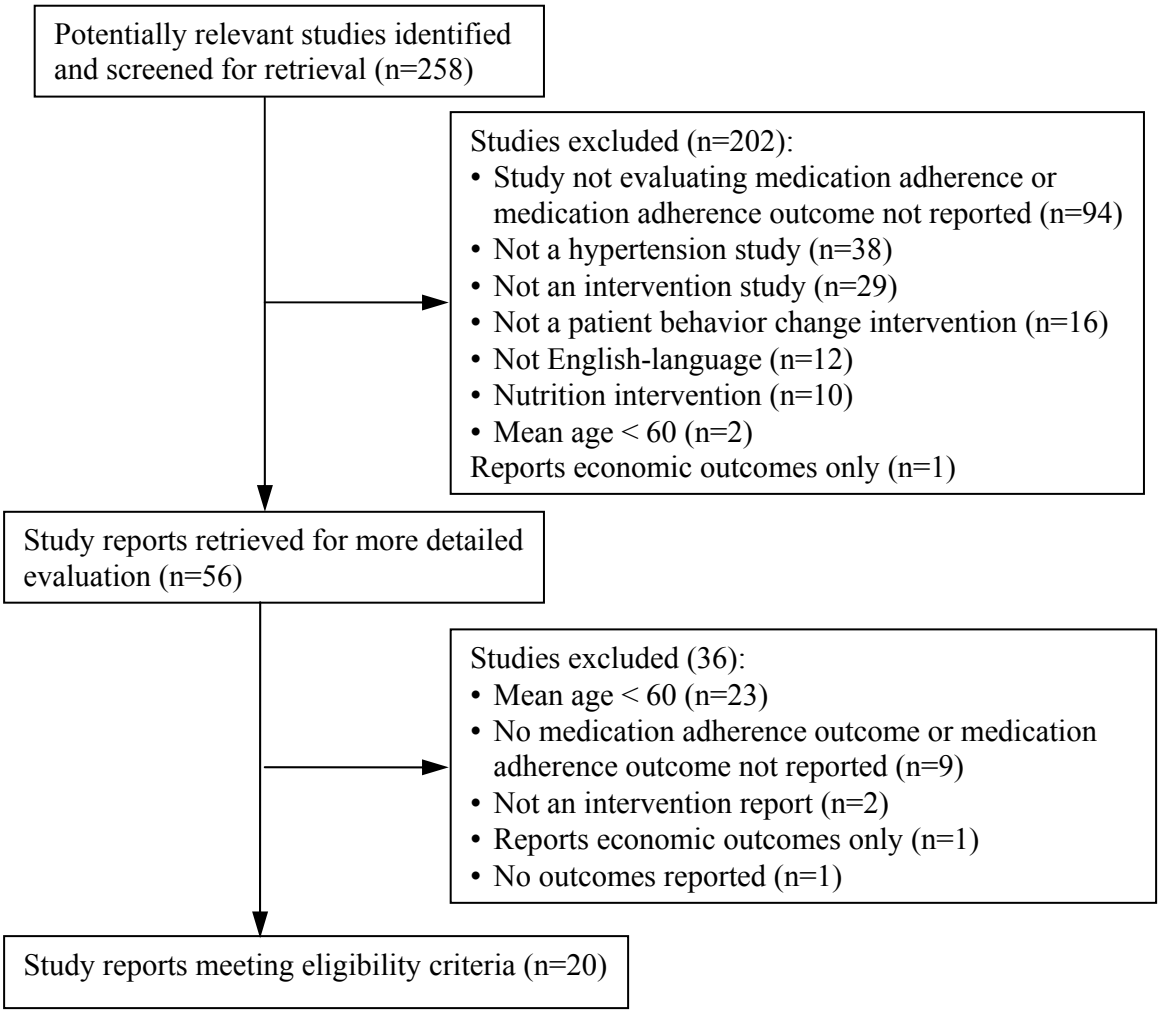


Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Blenkinsopp et al. (2000)	Controlled Trial (randomized by site) [UK]	• Medication education • Written information (Scriptographic booklet)	Contacts: 3 Duration: 2 months Mean min/visit: Visit 1: 11.54 Visit 2: 8.88 Visit 3: 7.74	Enrolled: 282 Tx: 167 Co: 115 Completed: Tx: 101 Co: 79	Not reported Over 60% of subjects age 60 or older	MA: % adherent (Tx: 62.9, Co: 50.0, $p < .05$) BP: NS in participants with controlled BP at baseline In participants uncontrolled at baseline (n = 28 Tx, 35 Co), % controlled at end of study was significant (Tx: 35.7%, Co: 17.1%, $p < .05$)	Self-report (MARS)
Boissel et al. (1996)	RCT [France]	• Dosing (BID vs. TID)	Contacts: 1 Duration: n/a (not a behavioral intervention)	Enrolled: 7274 Tx: 3638 Co: 3636 Completed: 6813	Tx: 61.3 (12.0) Co: 61.3 (12.0)	3 month outcomes MA: (% patients rating self as adherent): Tx: 82.3; Co: 71.2 ($p < .001$) BP: (% w/ controlled BP): Tx: 83.3; Co: 81.5 ($p = .049$) (negligible difference)	Self-report
Bosworth et al. (2005)	RCT [USA]	• Telephone nurse case management	Contacts: 12 (every 2 months) Duration: 24 months Mean call duration: 3.7 min.	Tx: 294 Co: 294	Tx: 63 (11.24) Co: 64 (11.48)	MA (after first 6 mo. of interv.): • Among participants adherent at baseline: Tx: 83% adherent vs. Co: 85%, ($p = 0.68$); • Among participants nonadherent at baseline: Tx: 46% adherent vs. Co: 34% ($p = 0.08$) BP: outcomes not reported	Self-report (Morisky scale)

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Burrelle (1986)	RCT (reporting only Phase 1 of a 2-group crossover design) [USA]	• Med education • HTN education • Packaging • Calendars • Written instructions (medication planners)	Contacts: varied Duration: 8 wks Mean min/visit: N/A	Enrolled: 16 Tx: 8 Co: 8	Tx: 68 Co: 70	At conclusion of intervention: MA: Tx: 92 ±4.57; Co: 71 ±12.06 ($p < .001$) BP: mean change (SBP/DBP) Tx: -13.25/-4.0, Co: -5.75/-11.25 ($p > .05$)	Pill counts
Chabot et al. (2003)	Nonrandomized quasi-experimental [Canada]	• Tailored based on adherence and BP at time of visit • BP & MA monitoring by RPh • education (HTN & med) • positive feedback • rewards • communication with provider	Contacts: mean of 5 contacts per subject Duration: 9 months Mean min/visit: N/A	111 enrolled; 100 completed study; Tx: 41 Co: 59	Tx: 68 Co: 63 ($p = .016$) 73% of subjects were ≥ 60 yrs.	MA (% of subjects adherent): High-income group: Tx: 85%, Co: 74% ($p = .067$) Low-income group: Tx: 32%, Co: 88% ($p = .095$) *Used $p < .10$ level of sig.* BP: high income group: SBP reduction: Tx: -7.8 ±2.9, Co: 0.5 ±2.0 ($p = .01$) DBP reduction: Tx: -6.5 ±1.8, Co: -4.0 ±1.2 ($p = .28$) Low income group: NS (data not reported)	Self-report (Morisky scale)

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
De Castro et al. (2006)	RCT [Brazil]	• Med education • HTN education • Identification of drug-related problems	Contacts: 3 Duration: 6 weeks (contacts at 0, 2, & 6 wks.) Mean min/visit: N/A	71 enrolled; 57 completed all visits; 64 included in ITT analysis Tx: 30 Co: 34	Tx: 63.9 (9.0) Co: 59.1 (10.1)	MA (4 months after completion of intervention): Tx: 78% vs. Co: 80% (p = .904) BP: NS (p-level not reported) • SBP change: Tx: 17 ±20, Co: 12 ±19; • DBP change: Tx: 10 ±10, Co: 6 ±14	Serum HCTZ level
Friedman et al. (1996)	RCT [USA]	• Self-monitoring of symptom (blood pressure) • Self-monitoring of medication • Medication education • Motivational counseling	Contacts: 26 (weekly) Duration: 6 months Mean min/visit: 4 min.	Enrolled: 299 Completed: 267 Tx: 133 Co: 134	76.0 yrs Tx: 76 Co: 77	MA (% improvement in adherence): Tx: 17.7, Co: 11.7 (p = .03) BP (change): SBP: Tx: 11.5, Co: 6.8 (p = .20) DBP: Tx: 5.2, Co: 0.8 (p = .02) when adjusted for age, sex, baseline MA & baseline BP	Pill counts
Girvin et al. (1999)	Randomized 3-phase crossover [Ireland]	• Dosing (QD vs. BID)	Contacts: 1 Duration: 12 wks of tx, 4 wks per phase Mean min/visit: N/A	Enrolled: 27 Completed: 25	62 yrs	MA (% doses taken, Tx vs. Co): Pill Count: 99 vs. 94.9 (p < .01) MEMS: 101.2 vs. 90.1 (p < .001) MEMS: (% correct dosing days): 92.2 vs. 72.6 (p < .001) BP: NS; SBP Tx: 124.7, Co: 122.7 (p = .182); DBP Tx: 76.5, Co: 75.2 (p = .275)	MEMS and pill counts

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Gonzalez-Fernandez et al. (1990)	RCT [Puerto Rico, USA]	• Educational interventions: 1. "knowing high BP" 2. "diet and high BP" 3. "exercise & high BP" 4. "meds & high BP"	Contacts: 4 Duration: 2 days Min/visit: 15-20 min	Enrolled: Tx: 30 Co: 29 At f/u: Tx: 25 Co: 22	Tx: 60 (10) Co: 58 (12)	8 weeks post-interv. MA: self-report success rates: Tx: 96%, Co: 36% (p = .04) Significant improvement from baseline only found in Tx group (30% to 96%, p < .001) BP: significant reduction in Tx group (p = .005) but not Co group (p = .63)	Self-report
Hunt et al. (2004)	RCT [USA]	• Mailed written HTN education materials Packet 1: intro letter, educational booklet w/ basic overview of HTN and lifestyle mod., fridge magnet reminding of target BP Packet 2: provider letter, educational booklet on med compliance, home BP monitoring, BP log	Contacts: 2 Duration: 3 months 0 mo.: Packet 1 3 mo.: Packet 2 Mean min/visit: N/A	302 in each group invited to participate Enrolled: Tx: 162 Co: 150	Tx: 69.2 (12.4) Co: 69.3 (12.3)	At 1 year (±3 months) MA: no significant difference (Tx: 0.35, Co: 0.35; p = ns) BP (mean BP Tx vs. Co): SBP: 135 ±14.7 vs. 137 ±15.4 (p = .229) DBP: 77 ±11.1 vs. 77 ±10.7 (p = .858)	Self-report (Morisky)

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Kim et al. (2006)	Single group pre-post [USA, focusing on Korean Americans]	• Structured, 2-hour weekly behavioral educ. sessions on mgmt of BP; CV risk factors & stroke prevention; mental health/ exercise; nutrition; meds; problem-solving & communication skills • Home BP monitoring • Monthly support groups (nurse-facilitated)	Contacts: 6 Duration: • Educ. sessions: 2 hrs/ wk for 6 wks • BP monitoring: 6 months • Support groups: Approx. 1 hour for each monthly group	Enrolled: 49 Intervention delivered to 31	68 (5)	6-month outcomes MA (lower scores indicate better adherence): baseline: 18 ±2.0 outcome: 23 ±6.0 (p = .142) BP (baseline vs. outcome): SBP: 141.7 ±9.1 vs. 129.3 ±3.1 DBP: 87.1 ±9.9 vs. 75.3 ±11.5 (p = ns)	Self-report (Hill-Bone Adherence of HBP Therapy Scale; measures more than just med adherence)
Lee et al. (2006)	Single group pre-post [USA]	• Medication education • Packaging (blister packs) • f/u w/ clinical pharmacist every 2 months	Contacts: 3 Duration: 6 months Mean min/visit: Initial visit: 1 hr f/u visits: 30 min	Baseline: 200 Enrolled: 174 Completed: 159	78 (8.3)	8-month outcomes (6 months after start of intervention) MA: baseline: 61.2% (±13.5) outcome: 96.9% (±5.2) (p < .001) Proportion of subjects who were adherent (pill count at 80% or higher) increased from 5.0% to 98.7% (p < .001) BP reduction (n=184): SBP: -3.3 (p = .02) DBP: -0.8 (p = .30)	Pill counts

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Marquez Contreras et al. (2005)	RCT [Spain]	Tx1: phone calls with med adherence feedback Tx2: mailed interv. with HTN education General med education	Contacts: 3 0, 7 wks, 15 wks for both Tx groups Duration: 17 weeks Mean min/visit: N/A	Enrolled: 636 Evaluable: 538 Tx1: 184 Tx2: 172 Co: 182	Tx1: 61.7 (12.3) Tx2: 59.3 (12) Co: 61.9 (10.6)	21-wk (post-intervention start) outcomes MA: Tx1 & Tx2 both showed signif. higher MA at f/u than Co group (p = .0001) BP: All groups decreased btw baseline & final. Only Tx1 had a signif. greater decrease compared to Co (31.6 vs. 22.1, p = .0001)	Pill counts

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
McKenney et al. (1992)	2-part RCT [USA]	Phase 1: Reminder/packaging: timepiece caps Phase 2: Tx1: timepiece cap Tx2: timepiece cap & pocket card for recording clinic BP measurements Tx3: timepiece cap, pocket card, & BP cuff for self BP monitoring	Contacts: not reported Duration: Phase 1: 12 wks Phase 2: 12 wks Mean min/visit: N/A	Enrolled: 70 Phase 1: Tx: 36 Co: 34 Phase 2: Co: 17 Tx1: 18 Tx2: 18 Tx3: 17	73.3	Phase 1: MA: (means) Tx: 95.1% vs. Co: 78% (p = .0002) BP: signif reductions in SBP & DBP in Tx group (p = .006 & p < .0001) , no signif reduction in Co group (p = .13 & p = .43) Phase 2: MA: All Tx groups were signif better than Co Tx1: p = .003 Tx2: p < .0001 Tx3: p < .0001 BP: (mean change) Co: NS (p > .50) Tx1: SBP -7.80 (p = .04); DBP -13.13 (p =.0001) Tx2: SBP -11.00 (p = .01); DBP -7.64 (p = .0001) Tx3: SBP -15.00 (p = .0006); DBP -6.60 (p = .0006)	Pill counts
Mehos et al. (2000)	RCT [USA]	• Self- monitoring of BP & self-monitoring of meds (missed doses) • Monthly or bi-monthly phone contact by RPh	Contacts: varied Duration: 6 mo. Mean min/visit: N/A	Enrolled: 41 Completed: Tx: 18 Co: 18	Tx: 60.0 (14.8) Co: 57.6 (13.5)	6-month outcomes MA: mean adherence 82% Tx, 89% Co (p = .29) BP: mean decr. (Tx vs Co): SBP: 17.1 vs. 7.0 (p = .069) DBP: 10.5 vs. 3.8 (p = .022) MAP: 12.7 vs. 4.9 (p = .01)	Prescription refills

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Mengden et al. (2006)	RCT [Germany]	• Interactive MEMS cap • HTN education - definition of normal BP - consequences of uncontrolled HTN - effect of adherence on HTN control - correct use of self BP monitoring	Contacts: 1 Duration: Interactive mems for 8 weeks Mean min/visit: 30 min. (educ. program at wk 0)	Enrolled: 44 Tx: 24 Co: 20	Tx: 64 (6) Co: 60 (10)	8-wk outcomes MA (mean, Tx vs. Co): 0.9973 vs. 0.9770 (p = ns) BP (mean decr. (Tx vs. Co): SBP: -9 ±11 vs. -10 ±16 (p = ns) DBP: -4 ±8 vs. -6 ±7 (p = ns)	MEMS
Schroeder et al. (2005)	RCT [Bristol, UK]	• Adherence support sessions to solve medication problems	Contacts: 2 Duration: 2 mo. Mean min/visit: 0 mo: 20 min.; 2 mo: 10 min.	Enrolled: 245 Tx: 128 Co: 117 Completed: 204 Tx: 110 Co: 94	Tx: 67.9 (10.3) Co: 68.2 (9.4)	6 month outcomes MA (mean, Tx vs. Co): 87.2 vs. 90.2 (p = .63) BP (mean, Tx vs. Co): SBP: 142.9 vs. 147.7 (p = .24) DBP: 80.4 vs. 79.9 (p = .85)	MEMS
Solomon et al. (1998)	RCT [USA]	• Medication and disease education • Medication review by pharmacist • Pharmacist involvement in health care team's management of care (collaboration with PCP)	Contacts: 5 Duration: 6 months Mean min/visit: N/A	Tx: 63 Co: 70	Tx: 66.3 (10.0) Co: 67.3 (11.0)	6 month outcomes MA (mean, Tx vs. Co): 0.23 vs. 0.61 (p = .007) BP (mean, Tx vs. Co): SBP: 138.5 vs. 144.9 (p = .044) DBP: 80.2 vs. 83.2 (p = ns)	Self-report (Morisky)

Table 1: *Characteristics of Reviewed Studies*

Author	Design [Location]	Intervention	Contact/duration	# subjects	Mean age (*SD*)	Outcomes	MA measure
Taylor et al. (2003)	RCT [USA]	• Pharmaceutical care - Medication education - med review by RPh - brief disease education	Contacts: not reported Duration: 12 months Mean min/visit: Approx. 20 min.	Enrolled: 81 Completed: Tx: 33 Co: 36	Tx: 64.4 (13.7) Co: 66.7 (12.3)	12 months (post-intervention start) MA: (all subjects, % adherent, Tx vs. Co) 100 vs. 88.9 (p = .115) BP: (nTx: 24, nCo: 29) % of patients at target BP: 91.7% vs. 27.6% (p =.001)	Self-report of missed doses
Vivian (2002)	RCT [USA]	• Drug counseling/ medication education	Contacts: 6 Duration: 6 months Mean min/visit: N/A	Enrolled: Tx: 27 Co: 29 Completed: Tx: 26 Co: 27	Tx: 64 (10.9) Co: 65.5 (7.8)	6 month outcomes MA: no significant difference btw Tx & Co (p = .252) BP (mean, Tx vs. Co): SBP: 130.5 vs. 148.4 (p = .0002) DBP: 77.5 vs. 80.4 (p = .259)	Self-report

Note: BP=Blood Pressure; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; MA=Medication Adherence; Tx=Treatment group; Co=Control group; NS=not significant; MARS=Medication Adherence Rating Scale; MEMS=Medication Electronic Monitoring System; Morisky=Morisky Adherence Scale

Study Design, Quality, and Theoretical Frameworks

Slightly more than half of the studies were randomized controlled trials (n = 12). Study design and quality assessments are listed in Table 2. The proportion of participants lost to follow-up at the time of outcome measurement ranged from 0% to 36.7%. Fifteen studies did not report using any theoretical framework to guide the design or delivery of the intervention. The remaining studies reported a range of theoretical models, namely the Health Decision Model (Bosworth, Olsen, Gentry et al., 2005), the PRECEDE-PROCEED model (Chabot, Moisan, Gregoire, & Milot, 2003), Braden's Self-Help Model of Learned Response to Chronic Illness Experiences (Kim, Han, Park, Lee, & Kim, 2006), Leventhal's Self-Regulation Model (Schroeder, Fahey, Hollinghurst, & Peters, 2005), and Social Cognitive Theory (Friedman et al., 1996).

Table 2: *Quality Assessment of Included Studies*

Study	Randomized	Losses to follow-up	Comment
Blenkinsopp (2000)	Yes, by site	102/282 (36.2%)	
Boissel (1996)	Yes	461/7274 (6.3%)	
Bosworth (2005)	Yes	None	
Burrelle (1986)	Yes	None	Phase 1 of a 2-group crossover design
Chabot (2003)	No	11/111 (9.9%)	
De Castro (2006)	Yes	14/71 (19.7%)	Included 64 participants in intent-to-treat analysis, net loss of 7/71 (9.9%)
Friedman (1996)	Yes	32/299 (10.7%)	
Girvin (1999)	Yes	2/27 (7.4%)	
Gonzalez-Fernandez (1990)	Yes	12/59 (20.3%)	

Table 2: *Quality Assessment of Included Studies*

Study	Randomized	Losses to follow-up	Comment
Hunt (2004)	Yes	n/a	
Kim (2006)	n/a	18/49 (36.7%)	All 18 withdrew prior to receiving intervention.
Lee (2006)	n/a	15/174 (8.6%)	
Marquez Contreras (2005)	Yes	98/636 (15.4%)	
McKenney (1992)	Yes	None	
Mehos (2000)	Yes	5/41 (12.2%)	
Mengden (2006)	Yes	None	
Schroeder (2005)	Yes	41/245 (16.7%)	
Solomon (1998)	Yes	None	
Taylor (2003)	Yes	12/81 (14.8%)	
Vivian (2002)	Yes	3/56 (5.4%)	

Adherence Measurements

Medication adherence measures varied among studies. Methods used included self-report (n = 9), pill counts (n = 7), electronic monitoring using the medication event monitoring system (MEMS) caps (n = 3), prescription refill data (n = 1), and serum drug level (n = 1). One study used both MEMS and pill counts. Each study's measurement method is reported in Table 1.

Effect on Medication Adherence and Blood Pressure Outcomes

Study results varied widely. Fourteen studies reported a statistically significant improvement in medication adherence, while thirteen reported a statistically significant improvement in blood pressure. A significant improvement in both medication adherence and blood pressure was reported in half of the studies. In a few studies, the outcomes,

while statistically significant, were not of a magnitude to be clinically relevant (e.g., a difference of less than 3 mmHg), or were significant for only a small subgroup of intervention subjects (Boissel et al., 1996; Chabot et al., 2003; Hunt, Siemienczuk, Touchette, & Payne, 2004). Some studies were underpowered for detecting changes in outcomes (de Castro et al., 2006) while other may have been overpowered to detect clinically meaningful changes.

Dose Modification

Two studies tested a dose modification intervention, whereby the number of daily doses of a medication is decreased. One study tested twice-daily versus three times per day, and the other tested once verses twice-daily dosing. Both studies found statistically significant improvements in medication adherence after three months (Boissel et al., 1996; Girvin, McDermott, & Johnston, 1999). Only one study reported a significant difference between groups in the percentage of participants with controlled BP, but acknowledged that the difference was small and could not be considered clinically significant (Boissel et al., 1996).

Packaging and Reminders

Packaging interventions commonly involve the use of a nonstandard medication container that is designed in some way to remind participants that medication needs to be taken or has already been taken. Packaging interventions included pillboxes (Burrelle, 1986), blister packs (Lee, Grace, & Taylor, 2006), and electronic medication caps with a reminder feature (McKenney, Munroe, & Wright, 1992; Mengden, Vetter, Tousset, & Uen, 2006). Three of the four studies (five of six total intervention groups) reported significant medication adherence outcomes (Burrelle, 1986; Lee et al., 2006; McKenney

et al., 1992). Only two studies reported significant blood pressure outcomes, and in one, significance was observed in systolic blood pressure only (Lee et al., 2006; McKenney et al., 1992).

Educational Interventions

The most commonly used intervention components were medication education (n = 13) and hypertension education (n = 10). Medication education commonly consisted of information about the prescribed medications, their purpose, dosage, and administration times. Often, medication education interventions also included information about potential side effects and interactions, and information about the importance of adherence to the therapeutic regimen. Eight of the thirteen studies using medication education significantly improved medication adherence.

Hypertension education usually consisted of general information about hypertension, its effects on the body, pharmacologic treatment strategies, and the potential consequences of inadequate blood pressure control. Four of ten studies using hypertension education reported significant adherence improvement. Only two of the ten hypertension education studies did not include a medication education component in the intervention. Those two studies did not report any improvement in adherence due to the intervention (Hunt et al., 2004; Mengden et al., 2006). In two other studies, hypertension education was specifically augmented with information about nonpharmacologic methods for controlling blood pressure, such as improving nutrition or exercise activity (Gonzalez-Fernandez, Rivera, Torres, Quiles, & Jackson, 1990; Kim et al., 2006). One study showed significant improvement in adherence and BP outcomes (Gonzalez-Fernandez et al.,

1990), but the other reported no significant improvement in either outcome (Kim et al., 2006).

Feedback and Support Interventions

Blood Pressure Monitoring. Six studies included some form of blood pressure monitoring as an intervention to improve medication adherence and blood pressure outcomes. In one study, the blood pressure monitoring was performed by study pharmacists as a feedback method in a multifaceted intervention program (Chabot et al., 2003). This study's intervention included medication and hypertension education and a system of positive feedback and rewards. Adherence and BP outcomes were improved for high-income participants, but not for low-income participants (Chabot et al., 2003). This finding is consistent with moderator analyses from a recent meta-analysis of medication adherence intervention studies, where interventions were found to be less effective in samples of older adults of lower socioeconomic status (Conn et al., in press). In the remaining five blood pressure monitoring studies, participants were provided with information on self-monitoring of blood pressure and were expected to check their own BP at home. (Hunt et al., 2004; Kim et al., 2006; McKenney et al., 1992; Mehos, Saseen, & MacLaughlin, 2000; Mengden et al., 2006). Little information was provided about the type or degree of information provided to participants in the five protocols. Only one of these five studies reported significant improvement in medication adherence and only two of the five reported significant differences in blood pressure control. These studies indicate the possibility that blood pressure monitoring may be more effective when performed by a health care provider, rather than when the participant is expected to self-monitor blood pressure.

Adherence Feedback. One study tested a telephone-mediated intervention in which, in addition to confirming participants' knowledge of their medication regimen, the nurse interventionists provided feedback on participants' level of medication adherence. Adherence information came from participant-performed pill counts. Participants who were adherent to their antihypertensive regimen were congratulated and encouraged to continue their good medication-taking behavior. Participants who were nonadherent were encouraged to improve their medication adherence, and were reminded of the health benefits of adhering to their antihypertensive regimen. Feedback phone calls were performed at three time points, spaced approximately seven to eight weeks apart. This simple intervention showed significantly better medication adherence and blood pressure outcomes when compared to the control group (Marquez Contreras et al., 2005).

Another study used positive feedback regarding participants' level of adherence and blood pressure control as a component in a multifaceted intervention. This study reported mixed results, achieving improvement in medication adherence and blood pressure control for higher-income participants; low-income participants experienced no improvement (Chabot et al., 2003). In this study, the adherence feedback was based on prescription refill data, which does not measure timing or daily dosing adherence. Additionally, the intervention was inconsistently delivered with variation in the number of intervention components used and the number of intervention contacts (Chabot et al., 2003).

Synthesis of Review

A variety of interventions exist with varied medication adherence and blood pressure control outcomes in older adults with hypertension. Dose reduction strategies

appeared to be effective, showing significant improvement in two studies at a level that would reach clinical relevance, ranging from an improvement of 11.1% to 19.6% over controls. These findings are consistent with findings of earlier reviews of medication adherence in hypertension and in older adults (Ruppar, Conn, & Russell, 2008; Schroeder, Fahey, & Ebrahim, 2004). Packaging interventions had statistically significant improvements in 75% of studies. Studies with significant outcomes showed improvement ranging from 17.1% to 35.7%. Education-based interventions, involving medication and/or hypertension education, had significant medication adherence improvement in 53.3% of reviewed studies. While this is a better rate of success than what has been found in other medication adherence reviews, it continues to indicate that educational interventions alone are likely insufficient to improve medication-taking behavior and may best be used as a component of a multifaceted intervention (George, Kong, Thoman, & Stewart, 2005; Haynes et al., 2005; Ruppar et al., 2008; Schroeder et al., 2004). Self-monitoring of blood pressure tended to be unsuccessful at improving medication adherence in older adults with hypertension, but feedback provided by a health care provider, particularly adherence feedback, showed promise as an intervention and would benefit from further testing in an older adult population.

Interventions varied widely by the number of contacts with the interventionist and the overall duration of the intervention. Not all intervention reports contained enough data to obtain an accurate assessment of the "dose" of the intervention for the purposes of comparison. For example, one study's intervention relied heavily on positive feedback and rewards, but the study report did not state how feedback was given, or what rewards were used (Chabot et al., 2003). Specific information about the intervention content,

duration, number of contacts, interventionist, and setting should be included in research reports to better facilitate the comparison of interventions.

Interventions addressing the development of medication-taking skills were notably missing from the literature. Such interventions, particularly those involving medication self-administration programs, have been shown to improve medication adherence in older adult populations (Russell, Conn, & Jantarakupt, 2006). One possible explanation for the absence of such studies from this review is that self-administration program interventions are commonly delivered in inpatient settings. Only one study in this review (Gonzalez-Fernandez et al., 1990) delivered an intervention in an inpatient setting. Additional research should address whether interventions to improve medication-taking skills are beneficial for older adults with hypertension.

Limitations

There are several limitations to this review. All reviewed studies were from English-language journals, which excluded a potential pool of reports. Additionally, no unpublished studies were identified. Additional search methods may locate unpublished studies meeting the review inclusion criteria. Because this review focused on medication adherence as an outcome, it necessarily excluded a number of hypertension intervention studies that may have had an effect on medication-taking behavior but did not measure it as a study outcome. Finally, the exclusion of studies where the treatment group mean age was less than 60 years may have eliminated studies with a significant proportion of older adults, but with a mean age just below the cutoff.

Comparison of outcomes of the reviewed interventions is difficult due to wide variation in interventions and outcome measures. No standards exist for measuring or

calculating medication adherence in patients with hypertension. Measurement tools range from self-report tools to high-tech electronic monitoring. Criteria used to objectively define what is adherent are often arbitrarily determined (e.g. 80% of prescribed doses in the past week, 75% of medications taken on time, etc.). The majority of studies used only one method of measuring adherence. Using multiple methods to measure adherence outcomes can improve outcome measurement precision and serve to cross-validate assessment tools. Multiple methods do, however, present challenges in interpreting study results.

The methodological quality of the reviewed studies varied. Not all studies included randomization, and several randomized studies did not adequately describe the randomization method. While blinding is quite difficult in behavioral studies, some study reports indicate potential for bias by having intervention and control participants seen by the same providers and failure to blind those performing data analysis. Additionally, fidelity to intervention protocols was not routinely discussed, and may vary among studies with similar interventions. Finally, only limited conclusions can be made due to the small number of studies in this review, particularly when discussing individual intervention categories.

Conclusions

The effect of educational interventions on medication adherence remains mixed. Hypertension education in the absence of medication education appears ineffective, even when in the presence of other intervention components. Conversely, adherence feedback shows potential for improving both medication adherence and blood pressure control.

Additional research is needed on adherence feedback, either as a standalone intervention or in conjunction with other intervention types.

Randomized Controlled Medication Adherence Intervention Trials in Older Adults

The number of antihypertensive medication adherence intervention studies conducted with older adult samples is limited. To provide additional background on medication adherence interventions among older adults, an additional review of the literature was performed, focusing on all randomized controlled trials of medication adherence interventions conducted with older adults.

Search Methods

Studies with interventions designed to increase medication adherence to prescribed medication regimens were included. Only randomized controlled trials were included to examine the most rigorous research in this area of science. Randomized controlled trials (RCTs) are preferred in that they maximize the ability to infer cause and effect outcomes (Cook & Campbell, 1979). Nonrandomized trials and single-group designs have greater threats to internal validity and thus, less generalizable findings (Cook & Campbell, 1979). Studies were included if the mean age of participants was 60 years or greater. Articles were identified for this study using computerized database searches, journal hand searches, and ancestry searches. Computerized database searches of English-language articles were conducted in MEDLINE (1965-2004), PsycINFO (1965-2004), HealthStar (1975-2004), Ageline (1987-2004), Cumulative Index of Allied Health Literature (CINAHL) (1982-2004) and the Cochrane Library (3rd Quarter 2004). These searches used the following keywords: *medication compliance, medication*

adherence, patient compliance, patient adherence, drug counseling, medication education, pharmacist counseling, pharmacist consultation, prescribed regimen, self-medication, and *pharmaceutical care*. Thorough searches through 2004 were performed on these databases by an expert health science information specialist, an approach that has been found to retrieve more eligible studies than using less experienced researchers (Conn, Isamaralai et al., 2003; Conn, Valentine, Cooper, & Rantz, 2003; Nony, Cucherat, Haugh, & Boissell, 1995). The search was recently updated to capture studies published in 2005. Hand searches were performed on journals in which the articles found in the computerized database searches were frequently published. Finally, ancestry searches were conducted on all eligible studies (Conn, Isamaralai et al., 2003).

Description of Studies

Study Characteristics

Of the 64 medication adherence intervention articles reviewed, two reported results from the same study, leaving 63 eligible studies for review. The studies were published between 1977 and 2005, with 4 studies from the 1970s, 13 from 1980 through 1989, 29 from 1990 through 1999, and 17 from 2000 through 2005. Two studies were unpublished doctoral dissertations (Halfmann, 2000; Kennedy, 1990). Total sample sizes in the reviewed studies ranged from 11 to 7,274 participants. The combined sample size of all of the reviewed studies was 15,520 participants.

Nearly all of the studies lacked a theoretical basis for the intervention. One study used the Transtheoretical Model (Friedman et al., 1996), one used the Theory of Reasoned Action (Halfmann, 2000), and one used Orem's Self-Care Deficit Theory (Kennedy, 1990).

Varied strategies, including human and technological, were used to intervene with medication adherence. Interventionists, or those delivering the medication adherence intervention, were most commonly pharmacists, nurses, physicians, or a combination of different disciplines. Three of the studies included use of a computer or automated voice technology. Of these three, all found significantly greater medication adherence among treatment group participants than those in the control group (Friedman et al., 1996; Leirer, Morrow, Pariante, & Sheikh, 1988; Leirer, Morrow, Tanke, & Pariante, 1991). Eighteen studies involved some degree of mediated intervention through telephone calls. Half of the mediated studies reported greater adherence in the experimental group.

Intervention Duration and Frequency

Intervention contacts, the amount of time spent during each encounter that the intervention was delivered, ranged from as short as three minutes to as lengthy as two hours. The total intervention duration ranged from a single contact to multiple contacts spread over as long as 29 months. Single contact interventions were common (n = 21 [33%]).

Intervention Setting

The interventions were delivered in a variety of settings. The settings can be broadly categorized into inpatient or outpatient. Medication adherence interventions were delivered to hospital inpatients in 20 of the 63 reviewed studies. Most of these involved medication adherence interventions to prepare patients to self-administer medications after discharge.

The remaining 43 studies involved some form of outpatient medication adherence intervention. Some interventions were based in ambulatory care clinics; some were based

in pharmacies. Three of the sixty-three reviewed studies utilized home visits as a means to deliver medication adherence interventions. Of the three, the only study reporting significant positive adherence outcomes used written information and packaging interventions in addition to medication education (Burrelle, 1986), while the other two used only medication education (Begley, Livingstone, Hodges, & Williamson, 1997; Sidel et al., 1990).

The majority of interventions involved only the individual patient. Only three of the sixty-three studies were directed at family or caregivers in addition to the individual (Al-Rashed, Wright, Roebuck, Sunter, & Chrystyn, 2002; Begley et al., 1997; Nazareth et al., 2001).

Content of Interventions to Improve Medication Adherence

A conceptual model of medication adherence interventions emerged during the review process. Each intervention in the reviewed studies addressed one of three factors affecting medication administration: (1) patient-focused factors (e.g., knowledge, skills, and attitudes about medication), (2) medication factors, and (3) administration factors.

Patient-Focused Factors

Patient-focused factors are those that affect participants' knowledge, skills and attitudes regarding taking medications. The interventions in this area are medication education, disease education, medication charts, self-administration programs, motivational counseling, social support, symptom monitoring, and self-management programs.

Medication education. Medication education was by far the most common strategy utilized among the reviewed interventions, being found in 45 of the 63 studies.

Twenty-two of the 45 studies reported significantly better adherence among treatment group participants as compared to control participants. Whether used alone or in combination with other intervention methods, most studies included some form of education about participants' prescribed medicines, medication schedules, and side effects. Several studies investigated structured medication education as part of discharge planning to improve post-discharge medication compliance (Al-Rashed et al., 2002; Edwards & Pathy, 1984; Faulkner, Wadibia, Lucas, & Hilleman, 2000; Foster et al., 1993; Jennings, Auckland, Franklin, Giles, & Austin, 1992; Kennedy, 1990; Laporte et al., 2003; Lipton & Bird, 1994; Lowe, Raynor, Purvis, Farrin, & Hudson, 2000; Nazareth et al., 2001; Pereles et al., 1996; Raynor, Booth, & Blenkinsopp, 1993; Rich, Gray, Beckham, Wittenberg, & Luther, 1996; Roden, Harvey, Mayer, & Spence, 1985; Smith et al., 1997). Medication education can range from simple verbal instructions of how to take medications, to detailed structured information on medications' purposes, side effects, correct use, and proper storage (Ascione & Shimp, 1984; Begley et al., 1997).

Methods of conducting medication education also varied among study interventions. While most medication education interventions used verbal, face-to-face methods (Blenkinsopp, Phelan, Bourne, & Dakhil, 2000; Cargill, 1992; Faulkner et al., 2000; Weinberger, Tierney, Booher, & Katz, 1991; Wood, 1989), others were telephone-mediated (Schectman, Hiatt, & Hartz, 1994; Smith et al., 1997; Weinberger et al., 1991), computer-mediated (Edworthy & Devins, 1999; Leirer et al., 1988), or audiotaped (Edworthy & Devins, 1999).

Written information. Thirteen of the sixty-three reviewed studies used some form of written information as a medication education delivery method. Eight of the thirteen

studies reported significantly greater adherence in the treatment group participants when compared to the control group. Written information was always used in conjunction with other interventions or forms of medication education. Some studies, however, were designed with multiple intervention groups, testing medication education with and without complementary written information, and also in conjunction with other interventions (i.e., reminder calendars, packaging) (Ascione & Shimp, 1984; Lourens & Woodward, 1994). Written information interventions generally consisted of medication cards or pamphlets containing generic and brand names of the participants' medicines, dosages, dosing schedule, interactions, side effects, purpose of the medication, and any special directions or precautions (Lourens & Woodward, 1994).

Disease Education. Disease education was used in five of the reviewed studies as an adjunct to medication education. Significantly better adherence from the intervention was reported in four of the five studies. Disease education focused on information about the participants' particular chronic diseases and the diseases' effective management (Paulós, Nygren, Celedón, & Cárcamo, 2005; Rich et al., 1996; Solomon et al., 1998; Sturgess, McElnay, Hughes, & Crealey, 2003; Wood, 1989).

Self-Administration Programs. Self-administration programs consisted of interventions designed to train individuals to correctly and reliably take their own medications. The four studies testing self-administration programs in this review were all inpatient programs designed to promote skill acquisition and behavioral training to prepare participants to successfully self-administer medications upon hospital discharge (Faulkner et al., 2000; Foster et al., 1993; Lowe, Raynor, Courtney, Purvis, & Teale, 1995; Pereles et al., 1996). The self-administration programs usually used graduated

stages of self-administration to monitor participants' abilities as they were given increasing responsibility for their medications (Lowe et al., 1995). Two of the four studies using self-administration programs reported significantly greater adherence outcomes in the intervention group.

Motivational counseling. Motivational counseling is a specific type of counseling intervention where individuals' motivation for a behavior is enhanced by exploring and resolving ambivalence. Only one of the reviewed studies included motivational counseling as part of its intervention, and reported significantly better adherence outcomes in the intervention group as compared to control participants. This particular study used a multifaceted approach, of which motivational counseling was a part (Friedman et al., 1996). The motivational counseling was delivered by an automated telephone system that used social-cognitive theory-based interactions with participants to promote the benefits of taking medication, promote self-efficacy for medication adherence, and provide positive reinforcement for improvements in adherence (Friedman, 1998; Friedman et al., 1996).

Social Support. Two reviewed studies included social support interventions. Neither study reported significantly improved adherence from the intervention. One study involved cardiac rehabilitation patients and consisted of monthly telephone calls from peers who were in a later stage of cardiac rehabilitation than the participant (Halfmann, 2000). The peer support calls included encouragement, empathic listening, and sharing of experiences and helpful tips for cardiac rehabilitation (Halfmann, 2000). The other study involved nurse-led peer support groups for people taking antihypertensive medications (Schroeder et al., 2005). The group sessions, led primarily by the patients, provided

participants an opportunity to discuss problems with their antihypertensive medications and allowed the nurses to help participants address medication problems (Schroeder et al., 2005).

Symptom Monitoring. Another intervention found in medication compliance intervention literature is symptom monitoring, where the participants monitored and recorded their own symptoms as part of a larger medication adherence program. Self-monitoring of symptoms is a mechanism for facilitating patients' involvement in their care (Varma, McElnay, Hughes, Passmore, & Varma, 1999). Of the three reviewed studies using symptom monitoring, all three reported significantly better adherence outcomes among intervention participants. Two studies had participants monitor their blood pressure (Friedman et al., 1996; McKenney et al., 1992) while the third had participants monitoring symptoms of congestive heart failure (CHF) (Varma et al., 1999). For one of the groups in the CHF study, the participants were given a protocol to follow for changes in specific CHF symptoms (e.g., marked increase in weight, increased shortness of breath, or increased ankle swelling) (Varma et al., 1999). The hypertension-oriented studies used the symptom monitoring as an outcome measure rather than as an intervention, although McKenney et al. (1992) found that the addition of blood pressure self-monitoring to their primary intervention (medication timepiece caps) contributed to improved medication adherence.

Medication Factors

Medication factors involved changes in the medication or its delivery that would impact participants' medication adherence. Such changes included adjustments in the medication dosing, packaging, or elimination of unnecessary medications.

Dose modification. Dose modification involves reducing the number of daily doses of the medicine. All six studies using this intervention reported significantly better adherence in the intervention group when compared to the control group. Dose modification was tested both as a standalone intervention (Boissel et al., 1996; Murray, Birt, Manatunga, & Darnell, 1993; Pullar, Birtwell, Wiles, Hay, & Feely, 1988) and as part of a multiple intervention medication adherence program (Brun, 1994; Girvin et al., 1999; Lowe et al., 2000). Dose modification interventions most commonly involved changing dosing from three times daily to two times daily, or from twice daily to once daily.

Packaging. Medication packaging as an adherence-promoting intervention consisted of two main types: containers and labeling. Medication containers to promote adherence generally consisted of pillboxes. Such pillboxes usually hold one week's worth of medication, divided up into one to four different dose administration times for each day. Another packaging option was the blister pack. Blister packs can hold medications, separated by dose, for a week or even a month on each package. Each blister may contain single or multiple medications. Labeling interventions may range from using larger print to improve readability, to adding more specific, lay language to the labels (Roden et al., 1985), or even using color-coded labels to denote the dosing times for the medicines in each bottle (Martin & Mead, 1982). Eleven of the sixty-three reviewed studies utilized packaging interventions. Four of the eleven studies reported significantly better adherence in the intervention group over the control group. In all but three of the eleven studies, the packaging intervention was coupled with other interventions.

Medication Review. Six of the reviewed studies that were primarily structured around other interventions also had participants' medication regimen reviewed by a health care professional. Two of the six studies reported significantly better adherence in the intervention group participants. The professional medication review, usually conducted by a pharmacist, was completed to determine inappropriate medications, medication interactions, and the need or possibility for dosage adjustments or frequency changes. Recommendations were made for any changes in the participants' medication regimens that might promote medication adherence by simplifying the regimen or lessening adverse effects.

In two of the reviewed studies, autonomous non-physician providers were used in addition to medication review. These are interventions where specific chronic conditions—in these studies it was hypertension and diabetes—are managed by a non-physician provider who, working within practice guidelines, implement a different approach to patient education and care from the perspective of that discipline. In the case of these two studies the provider was a pharmacist, and medication review for optimization of participants' medication regimen played a part in the overall intervention delivered by the pharmacist to increase medication adherence.

Administration Factors

Administration factors are those that are concerned with changing aspects of medication administration. Such interventions would include medication reminders and medication monitoring.

Medication reminders. A number of studies investigated the use of medication reminders to improve medication adherence. Medication charts or calendars are found in

nine of the sixty-three studies reviewed. Seven of the nine reported significantly better adherence among intervention versus control participants. All but one of the nine studies used this intervention in conjunction with other medication adherence strategies (Gabriel, Gagnon, & Bryan, 1977). Seven of the nine used medication charts or calendars in conjunction with medication education (Ascione & Shimp, 1984; Goodyer, Miskelly, & Milligan, 1995; Hanlon et al., 1996; Kennedy, 1990; Lowe et al., 2000; Raynor et al., 1993; Wandless & Davie, 1977). For example, Goodyer et al. (1995) used medication calendars as part of a standard medication counseling protocol employing the calendars plus verbal medication education, and written leaflets.

In some cases, the medication calendars or charts were used only when it was determined that the participant needed that part of the intervention. In Hanlon et al. (1996), the medication calendars were part of a larger intervention looking at the effect of a clinical pharmacist on care within a Veteran's Affairs Medical Center. In that study, the calendars were only used when determined appropriate by the clinical pharmacist (Hanlon et al., 1996). In Kennedy (1990), the medication calendar was combined with a medication self-monitoring tool, and was included as one part of a multifaceted intervention program when triggered by a participants' assessment score falling within a particular range (Kennedy, 1990).

Another type of medication reminder is the subcategory of stimulus control. Stimulus control involves something that cues or prompts patients to maintain adherence to a medication regimen (Fulmer et al., 1999). This can be done either by cueing to take medications or to refill prescriptions. Three of the 63 reviewed studies utilized a form of

stimulus control, with two reporting significantly better adherence in the intervention group.

Fulmer et al. (1999) investigated using daily telephone calls versus daily video-telephone calls as a stimulus control for directly administering medications. Another study used voice mail reminders for medication administration (Leirer et al., 1991). Simkins and Wenzloff (1986) investigated stimulus control for refilling prescriptions. They utilized postcard reminders sent to arrive two working days prior to the refill due date and a phone call reminder one working day prior to the refill due date (Simkins & Wenzloff, 1986).

Medication monitoring. Five studies used some form of monitoring for correct medication administration, with three reporting significant improvements in medication adherence among the intervention group participants versus the control group (Friedman et al., 1996; McKenney et al., 1992; Varma et al., 1999). Two studies utilized self-monitoring of medications, where the study participants kept track of their medication usage (Friedman et al., 1996; Varma et al., 1999); two used monitoring performed by the research staff as part of a multifaceted adherence intervention or medication self-administration program (Fulmer et al., 1999; Nazareth et al., 2001); and one used a device, timepiece caps, along with self-monitoring of blood pressure as interventions to improve medication adherence (McKenney et al., 1992). The participants could refer to the timepiece caps to see when they had last opened the bottle to take their medication. None of the studies reviewed used medication monitoring as a standalone intervention.

Synthesis of Review

The reviewed studies provide examples of twelve different interventions that may be used to promote medication adherence in elderly adults. Most interventions are geared to improving knowledge and skills for taking medications. Generally reports provide scant information about the nature or "dose" of medication education. Specific information about content, format, order of presentation, medium, interventionist, and duration, should be provided in reports of educational interventions (Conn, Cooper, Ruppar, & Russell, 2008). Randomized controlled trials comparing educational interventions would be helpful.

Most interventions to improve medication adherence have a medication knowledge component, to get patients to better learn and understand their medication regimens. Educational interventions can often be combined into multifaceted interventions, promoting change in multiple factors affecting medication adherence (Haynes et al., 2005). Unfortunately, while some experts assert that medication knowledge may be prerequisite for adherence, it is often not sufficient (George et al., 2005; Haynes et al., 2005). Fewer interventions involved medication factors or medication administration factors, although these are clearly important aspects of medication adherence.

Older adults often report forgetting as a common reason for missed doses (Conn et al., 1994). This is true regardless of the presence or absence of cognitive impairment. Yet few studies have tested interventions that address the tendency to forget medications. Only 12 of the reviewed studies involved medication reminders as an intervention component. More research is needed testing prompts to stimulate mediation taking

behavior at the time medications are prescribed to be administered. Several electronic devices have been developed to prompt and monitor medication administration; rigorous trials testing these devices need to be completed. Self-monitoring of medication consumption has received little attention. Self-monitoring of health behavior has been found effective for some other behaviors (Conn, Valentine, & Cooper, 2002). Further research testing interventions deliberately designed to test such self-monitoring could be informative (McKenney et al., 1992).

System factors also play an important role. The RCTs reviewed in this paper fail to adequately address health care system-level interventions. Medication adherence may be negatively impacted by lack of access to medicines, either due to cost or drug availability. Appropriate medication-taking also requires health care providers to improve communication and continuity of care, to prevent multiple providers prescribing duplicate therapy, or creating drug-drug interactions. Providers caring for older adults must also be aware of concerns related to polypharmacy and medications that are inappropriate in the elderly, due to physiologic changes associated with aging (Fick et al., 2003). Health care system interventions will necessarily vary due to innate differences in each nation's health system and may ultimately involve changes in public policy, but are an important component in improving medication adherence.

Most interventions have targeted older adults without involving family or other persons that might assist with medication adherence. Many older adults have informal caregivers that may assist with medications (Conn et al., 1994). Tests of interventions targeting the social context where medication adherence may occur, including informal caregivers, are needed. The small number of trials of interventions that include caregivers

indicates a strong need for research into interventions that are not strictly focused on the individual, but also include families and caregivers.

Theory-guided interventions may be better at including all aspects of medication adherence. Only three of the reviewed studies had a theoretical foundation for their interventions. Theory-based interventions may be better at addressing not only the need for medication education and reminders, but also the effect of perceived benefits and barriers, prior medication experiences, cultural factors, personal beliefs, side effects, readiness to change behavior, and the effect of health care system-level interventions. Theory-based interventions may better facilitate the use of interventions tailored to the individual's reasons for medication nonadherence.

Published research has treated medication adherence as a unitary construct. Little is known about variations in medication adherence beyond the rates of adherence reported in some studies. Patterns of adherence need to be studied (Russell et al., 2006). Older adults who are routinely late with doses probably need different interventions than those who miss entire doses. Older adults who intentionally take less medication than prescribed need very different interventions than those who intend to take medication as prescribed but often forget doses. By analyzing adherence data and providing feedback to participants as part of the intervention, it is possible to address individual patterns of adherence.

Limitations

This review was limited in that the papers reviewed were all from English-language sources and were from studies carried out primarily in the United States, the United Kingdom, and Australia. The papers reviewed do not include interventions that

may affect medication adherence without specifically targeting it, such as many types of chronic illness self-management programs. Some of the intervention components were tested in only a small number of RCTs, and all interventions were implemented in a variety of ways. This makes it difficult to make conclusions about the effectiveness of any single medication adherence intervention. Additionally, our focus on older adults may have led to the exclusion of studies with a sample mean age <60, but which still contained a significant number of elderly participants.

Conclusions

Medication adherence is a problem facing health care providers around the world. Despite pharmacological advances, many people continue to suffer health and well-being problems at least partially attributable to poor medication adherence. While common interventions such as medication education have been well-tested and clearly show benefit, some interventions found in the reviewed studies have been tested in very few clinical trials of medication adherence. Further research of culturally-competent, theory-driven interventions including long-term outcome measures is needed to evaluate the efficacy and practicality of several of these medication adherence interventions, including the international applicability of the interventions to diverse health care systems. Lastly, more randomized clinical trials are also needed of interventions delivered by nurses, who deliver a sizable portion of the medication adherence interventions in clinical practice but were surprisingly under-represented in the research found for this review.

Cognitive Outcomes in Antihypertensive Adherence Intervention Studies

Medication adherence is influenced in part by cognitive factors. Knowledge of the medication regimen is essential to proper medication adherence. If an individual does not know his or her medication dose and when the medication should be taken, he or she can not be expected to successfully adhere to the regimen. However, improving medication knowledge alone has been shown to be insufficient in improving medication adherence.

Beliefs and attitudes about the medication regimen are also important to the determination of successful adherence. If an individual does not believe a medication is effective or appropriate, he or she may voluntarily choose not to adhere to the regimen (Pound et al., 2005). Such medication beliefs and attitudes have been shown to be related to medication adherence behavior, but measures of medication beliefs have been underrepresented in adherence research (Horne & Weinman, 1999; Ross, Walker, & MacLeod, 2004). Among the 20 antihypertensive medication adherence intervention studies focusing on older adults, five studies reported measures of cognitive outcomes, with only two addressing participants' beliefs or attitudes about their medication regimens. The five studies' cognitive outcomes are summarized in Table 3.

Results among the five studies were mixed. No studies used instruments that comprehensively measured medication beliefs. Comparison of studies is confounded by variation in investigator-developed measures.

Table 3: *Cognitive Outcomes in Antihypertensive Adherence Intervention Studies*

Author	Medication Belief Outcomes	Measure
Bosworth et al. (2005)	Knowledge - Tx: 1.0 vs. Co: 1.0; $p = .49$ Confidence with HTN regimen - Tx: 0.33 vs. Co: -0.10; $p = .007$	Modified HTN beliefs questionnaire Investigator-developed scale
Burrelle (1986)	Knowledge and attitudes about HTN and antihypertensive therapy - Tx: 96.5 ±3.74 vs. Co: 73.5 ±13.23; $p < .001$	Investigator-developed scale
Hunt et al. (2004)	Knowledge - Tx 7.48 ±1.6 vs. Co: 7.09 ±1.6; $p = .019$ - Tx 7.6 ± 1.6 vs. Co: 7.09 ±1.6; $p = .003$ in Tx group participants who recalled receiving at least part of intervention	Investigator-developed scale
Kim et al. (2006)	HTN Knowledge - pre: 14.1 ±2.0, post: 14.7 ±2.3; $p = .19$	Items from NHLBI instrument
Taylor et al. (2003)	Medication knowledge (change scores at 12 months) - Tx: 36% vs. Co: -15%; $p < .0001$	Investigator-developed scale

Note: HTN=Hypertension; Tx=Treatment group; Co=Control group

Large changes in medication knowledge may have an effect on medication adherence and blood pressure outcomes. Taylor, Byrd, and Krueger (2003) found that participants receiving their tailor pharmaceutical care intervention had both significant improvement in knowledge of their medication regimen and in blood pressure outcomes. Other studies, reporting smaller changes in measures of medication knowledge did not have significant differences in adherence or blood pressure (Bosworth, Olsen, & Oddone, 2005; Hunt et al., 2004). These interventions used mailed materials that provided general

education about antihypertensive medications. Neither mailed intervention provided tailored education about participants' specific medication regimen.

Adherence interventions may have more consistent effects on measures of confidence in antihypertensive medication regimens and attitudes about hypertension and antihypertensive medications (Bosworth, Olsen, & Oddone, 2005; Burrelle, 1986). The study by Bosworth and others (2005) reported a significant change in participants' confidence in their antihypertensive medication regimen. The authors also found the intervention to significantly improve medication adherence among participants who were nonadherent at baseline. Burrelle (1986) found significant differences in a measure of knowledge and attitudes about hypertension and antihypertensive treatment. Intervention group participants in Burrelle's study also had significant improvement in medication adherence when compared to control group participants.

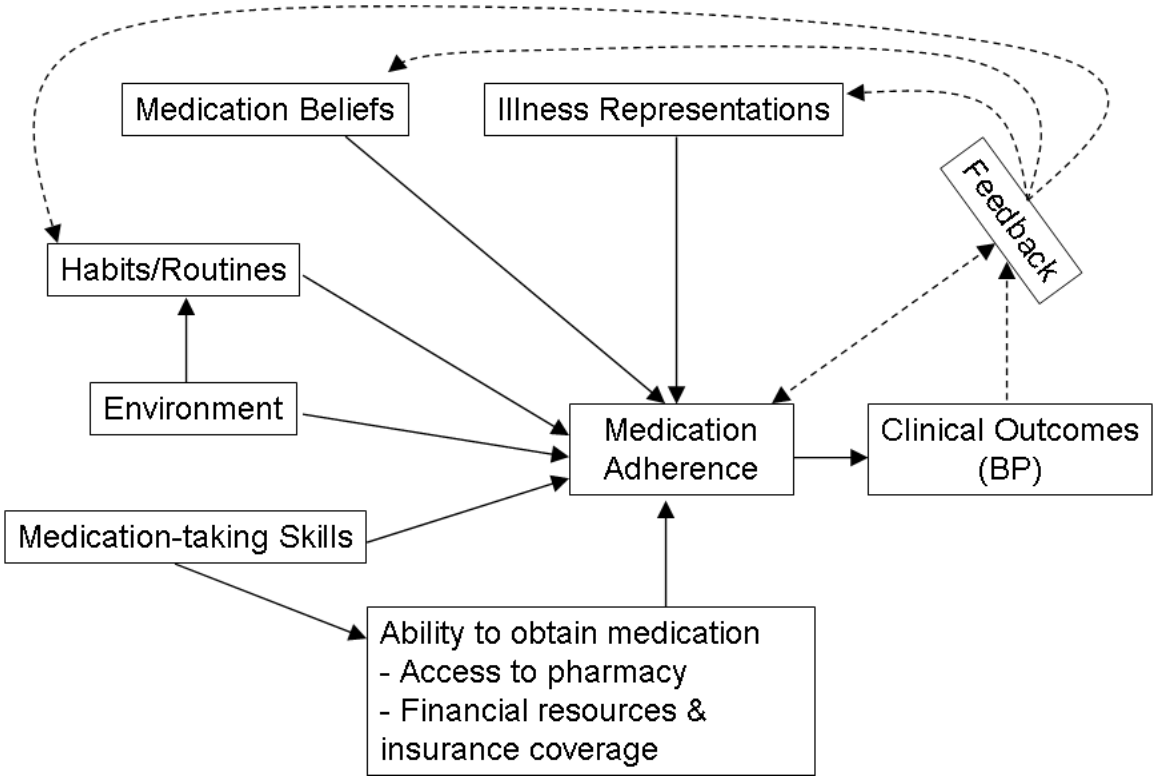
Medication knowledge is inconsistently related to medication adherence, but is important as a basis on which medication beliefs and attitudes are formed (Conn et al., in press). Medication and disease education may modify incorrect medication beliefs to improve medication adherence. No published studies currently address whether modification of older adults' medication beliefs as part of a comprehensive medication adherence intervention influences antihypertensive medication adherence. Further study is needed to evaluate these relationships in an intervention setting.

Conceptual Framework

Most medication adherence intervention reports do not cite any theoretical guidance for the intervention approach used (Ruppar et al., 2008). Thus, there is little

evidence to support one conceptual approach over another. Much of the medication adherence descriptive research reported to date focuses primarily on cognitive influences on adherence behavior. Recent meta-analytic work, however, demonstrates the importance of behavioral factors on medication adherence (Conn et al., in press). For this study, a conceptual model was developed to permit the use of intervention approaches impacting multiple dimensions of adherence behavior. A diagram of the framework components is shown in Figure 2.

Figure 2: *Conceptual Framework*



Cognitive Influences on Medication Adherence

The cognitive components of the conceptual framework are adapted from Leventhal's Self-Regulation Model (SRM), also known as the Common-Sense Model. In

the SRM, health behaviors are determined by an individual's illness representations, which include all things the individual knows, experienced, or is experiencing about their illness, and how that knowledge or experience is interpreted (Leventhal, 1983; Leventhal, Nerenz, & Straus, 1982; Leventhal, Zimmerman, & Gutmann, 1984). Illness representations also include the individual's beliefs about the expected cause of the illness, expected illness duration, beliefs about negative effects from the illness, and beliefs about the potential for treatment.

The SRM acknowledges that some illnesses do not have overt symptoms. This is usually the case for hypertension. Without an abnormal blood pressure measurement, a person may not have any noticeable symptom of hypertension, despite the damage the elevated blood pressure may be causing to multiple organ systems. Even for those illnesses with symptoms, the symptoms may not be recognized or may be misattributed to a different cause. As such, people may develop inaccurate or unrealistic illness representations. Accurate or not, individuals' health behavior is driven by their perceived symptoms. These health behaviors include medication adherence, which has been shown to be related to individuals' illness representations for the condition being treated (Horne & Weinman, 2002; Ross et al., 2004) Thus, it is important to understand how the person experiences and interprets symptoms.

Symptom Appraisal

Upon experiencing a symptom, an individual will interpret that symptom based on their current illness representation (beliefs and expectations about the illness) and their perception of whether the symptom is related to the illness, and whether the symptom is a threat. This process of symptom appraisal is how individuals assign meaning to

symptoms, determining whether the symptom is considered a threat, and whether action is required. Meaning is assigned through two parallel processes: objective, which are conscious perceptions and interpretations guided by knowledge and objective information; and subjective, which are the unconscious emotional reactions to the symptom. Both objective knowledge and emotional reactions have been shown to be influential in medication adherence behavior in individuals with hypertension (Ross et al., 2004).

Medication Beliefs

Psychological research on medication adherence has shown that people may experience a struggle between their beliefs about the necessity of medications and concerns about the negative effects of medications (Horne, Clatworthy, Polmear, & Weinman, 2001; Horne & Weinman, 1999; Ross et al., 2004). Significant relationships have been shown across chronic illness populations between good medication adherence and high scores on measures of belief in the necessity of medications, and with poor medication adherence and high scores on measures of concerns about medication-taking (Horne & Weinman, 1999; Llewellyn, Miners, Lee, Harrington, & Weinman, 2003; Ross et al., 2004).

Behavioral Influences on Medication Adherence

Health behaviors also have a distinct behavioral component. Daily routines and habits are important in the adoption and maintenance of health behaviors (Alemi et al., 2000). This is particularly true for a behavior such as medication-taking, which must be done every day, and generally at the same time(s) every day. An intervention model for

medication adherence must address both current habits, as well as the desired habitual behavior the intervention hopes to create.

Likewise, medication adherence cannot be improved if an individual lacks the necessary skills for taking medication. Simple skills such as the manual dexterity needed to open a pill bottle, the ability to count out the correct number of pills, or being able to arrange for medication refills when needed are important to achieving medication adherence. Functional changes that often occur as individuals age can impact the ability to execute these medication-taking skills.

Environment

Environmental factors also influence an individual's ability to adhere to a medication regimen. Environmental factors include everything from where an individual stores medications in their home, to health system issues involving access to prescription drug coverage and the individual's proximity to health care providers and pharmacies. Environmental factors can also include stimuli, either naturally-occurring or established by the individual, which serve as reminders to take medications.

Feedback

Frequently, individuals are unaware of how well they are adhering to their medication regimen, and whether they are meeting the desired clinical outcome. In many cases, improvement in physical symptoms can serve as a means for clinical feedback, but not all chronic conditions have perceptible symptoms that may be associated with illness control (Leventhal et al., 1984). This lack of symptom feedback can lead individuals to discontinue necessary medications (Johnson, Williams, & Marshall, 1999).

Summary: Modifying Adherence Behavior

Illness representations, symptom appraisal, medication beliefs, daily routines, medication-taking skills, and environmental factors all influence individuals' adherence to medication regimens and are all open to modification through intervention. The model then incorporates an evaluation component, where an individual evaluates—both objectively and subjectively—the effectiveness of their coping interventions. These evaluations provide feedback that can lead people to self-modify their illness representations, modify adherence behavior, and potentially how they evaluate their adherence and health in the future.

CHAPTER THREE: METHODS

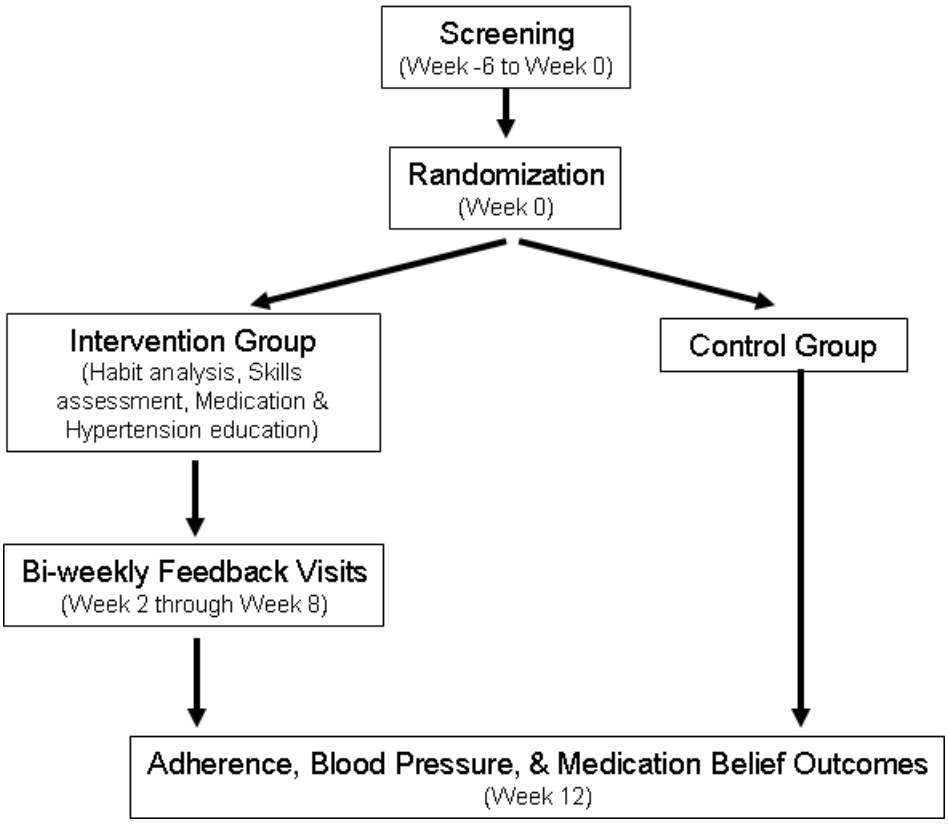
Design

This randomized, controlled, exploratory study tested an eight-week medication adherence intervention consisting of medication and blood pressure education, medication adherence feedback, and blood pressure feedback in a group of 15 older adults who were nonadherent to their antihypertensive medication regimens. Participants were recruited, oriented to the study, and informed consent was obtained. Participants' current medication regimens were documented. Baseline blood pressure measurements and beliefs about medications were assessed. Participants were then randomly assigned to intervention or control groups. Participants were followed in the study for a total of 12 weeks (four weeks beyond the end of the intervention), at which time final measurements of medication adherence, blood pressure, and medication beliefs were obtained (See Figure 3).

Setting

This study was conducted in the St. Louis, Missouri and Columbia, Missouri areas. Study visits occurred in the homes of community-dwelling older adults. For the purposes of this study, community-dwelling was defined as living in a home (house, apartment, condominium) or in a congregate-living environment (e.g. assisted living) where the participant remained responsible for administering his or her own medications.

Figure 3: *Participant Flow Chart*



Participants

This study enrolled community-dwelling elderly who were receiving medication therapy for hypertension. Study inclusion criteria were as follows:

1) Participants were aged 60 years or greater at time of study entry.
2) Participants were able to read, write, and converse in English.
3) Participants had a diagnosis of hypertension (based on participant report).
4) Participants had an active prescription for at least one antihypertensive medication with no antihypertensive prescription changes for 30 days at the time of study entry. See Appendix B for a listing of antihypertensive medications and medication classes.

5) Participants self-administered his or her own medications without prompts from any other person or device.
6) Baseline medication adherence rate of < 85%.
7) Participants were free of cognitive deficit as determined by a score of "normal" (0 – 2) on the Short Portable Mental Status Questionnaire (SPMSQ).
8) Participants agreed to complete all study contacts and measurements, including using a special medication bottle with a Medication Event Monitoring System (MEMS) cap for the duration of the study.
9) Were able to open and close MEMS caps.

Exclusion criteria:

1) Participant was in state of severe hypertension (BP of >180/120 mmHg) at the time of study enrollment. Participants presenting with severely elevated blood pressure were referred to their primary care provider.
2) Participant resided in a residential facility where medications were administered by facility staff. Participants who resided in assisted living facilities but maintained control of their medications remained eligible.
3) Participant had a terminal chronic illness with a life expectancy of six months or less.

Targeting the intervention to participants with adherence difficulty permitted the possibility of detecting an effect from the intervention, without confounding from ceiling effect. The necessary adherence level for antihypertensive medication effectiveness is not conclusively known, but preliminary research suggests 92% as an approximate cutoff

(Burnier, Schneider, Chiolero, Stubi, & Brunner, 2001). An adherence eligibility cutoff of 85% ensured participants were below the suggested adherence level for antihypertensive medication benefit, while potentially above the average level of adherence in the hypertensive and older adult populations (Botelho & Dudrak, 1992; Burnier et al., 2001; Cramer, 1998; van Eijken et al., 2003). The number of potential participants necessary to screen to enroll 15 older adults with <85% adherence was not known, but reported mean adherence rates are 76% among adults with hypertension and range between 26% to 59% among older adults in general (Botelho & Dudrak, 1992; Cramer, 1998; van Eijken et al., 2003). The recruitment and eligibility rates in this exploratory study provided important data for designing the planned larger study.

Sample Size

Due to the exploratory nature of this study, the sample size was limited to 15 participants, with 10 intervention group and 5 control group participants. This study was not powered for statistical tests of significance.

Measures

Measurements included screening assessments to determine eligibility and outcome measurements to evaluate the effect of the intervention (See Table 4). The research instruments used are described in the following sections. Copies of the instruments can be found in the appendices.

Table 4: *Study Concepts, Measurement Tools, and Definitions*

Concept	Measurement Tool	Operational Definition
Cognitive function	Short Portable Mental Status Questionnaire	Score of 2 or less indicates no impairment
Medication beliefs	Beliefs About Medications Questionnaire	A higher score indicates stronger beliefs on each subscale.
Medication adherence	MEMS and MEMS diary	The percentage of antihypertensive medication doses taken within prescribed intervals
Blood pressure	Aneroid sphygmomanometer	Blood pressure below 140/90 is considered controlled.

Cognitive Function

Cognitive function was screened at study enrollment only, using the Short Portable Mental Status Questionnaire (SPMSQ). The SPMSQ is a ten-item screening tool designed to distinguish between normal cognitive function and varying levels of intellectual impairment (Pfeiffer, 1975). This instrument has been used in both clinical and research settings, including thousands of elderly research study participants with test-retest correlation of 0.82 (Fillenbaum, Heyman, Williams, Prosnitz, & Burchett, 1990; Pfeiffer, 1975). The instrument tests several aspects of orientation and memory, as well as a test of executive function. Scoring is performed by summing the number of errors made and adjusting for the participant's educational level.

Beliefs About Medications

Participants' medication beliefs were assessed using the Beliefs About Medications Questionnaire (BMQ). The BMQ is a ten-item scale that measures beliefs about participants' medication regimens. The BMQ is divided into two subscales, one measuring beliefs about the necessity of medications, and the other measuring concerns about taking medication. All items are answered on a five-point Likert scale, ranging

from 1 (strongly disagree) to 5 (strongly agree). Scores on each subscale are summed, and can then be used to calculate a necessity-concerns ratio as a guide to the relative strength of participants' beliefs about the necessity of their medications and the benefit they receive from them, versus concerns about dependency and problems arising from medication use (Horne, Weinman, & Hankins, 1999; Neame & Hammond, 2005). Internal consistency alphas during instrument development ranged from 0.55 to 0.86 across diverse patient populations (Horne et al., 1999). Test-retest correlation was 0.77 for the necessity subscale and 0.76 for the concerns subscale. 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. Data collected with this tool provides reliability data from this specific population to use in developing future studies.

Medication Adherence

The Medication Event Monitoring System (MEMS, Aprex Corp., Union City, CA, USA) was used as the primary measure of antihypertensive medication adherence. The MEMS are medication bottle caps with an implanted RFID chip that records a date/time stamp each time the pill bottle is opened. MEMS caps have been shown to be reliable in temperatures ranging from -20°C to 70°C and in up to 95% humidity (Dunbar-Jacob, Sereika, Foley, Bass, & Ness, 2004). The caps have a 36-month battery life, are accurate to within 2 minutes per month, and have a reported failure rate of 2% (Dunbar-Jacob et al., 2004; Russell et al., 2007). Data stored on the MEMS cap are downloaded via a specialized cap reader to a computer, where it is stored in proprietary data management software (PowerView, Aprex Corp., Union City, CA, USA) that facilitates

data cleaning and calculation of medication adherence rates. Data can then be exported as needed to other data management software.

The MEMS is widely recognized as one of the best methods for measuring medication adherence, as it monitors the date and time the medication bottle is opened to remove the medication. This permits accurate monitoring of the timing of medication removal and permits analysis of adherence patterns. The caps are limited in that, like most methods of medication measurement, it cannot determine whether the medication was actually consumed. The cap also cannot distinguish between purposeful and accidental openings. To account for this, multiple openings within a 15-minute interval were eliminated from data analysis. Participants were also provided with a diary card (see Appendix E) on which to record any accidental MEMS bottle openings or openings for purposes other than medication taking (e.g. medication refill). Such additional or accidental openings were excluded when computing adherence rates. If the participant was hospitalized during the study, the hospitalization time where the participant was not self-administering medications was excluded from computing medication adherence rates.

Each participant was given one MEMS cap and bottle to use for their antihypertensive medication. If the participant was taking more than one daily antihypertensive medication, the MEMS was used with the antihypertensive medication with the greatest number of prescribed daily doses. This permitted the adherence measurement to match the complexity of the participant's antihypertensive medication regimen. If the participant used a pillbox for organizing medications (or began to use a pillbox as part of the study intervention) the participant was provided with "Tic Tacs®" to

place in the pillbox as a reminder to obtain the medication from the MEMS bottle. This method has been used successfully in previous research (Russell et al., 2007). A Tic Tac® is a mint candy with less than 0.5 mg of sugar per piece. Participants were instructed to use the Tic Tacs® as placeholders in their pillboxes, and that the Tic Tacs® were not intended to be consumed.

Blood Pressure

Resting blood pressure was measured per American Heart Association guidelines on the participants' left upper arm using an aneroid sphygmomanometer and stethoscope auscultation of the brachial artery. The right arm was used if use of the left arm for blood pressure measurement was contraindicated in a particular participant. Systolic and diastolic blood pressure was recorded as the sphygmomanometer reading corresponding with the first and fifth Korotkoff sounds, respectively (Pickering et al., 2005). Blood pressure was measured with the participant in a seated position after at least 10 minutes without ambulation. The lower arm was held below heart-level and supported on a table, armrest of a chair, or in the participant's lap. The same investigator conducted all blood pressure measurements on all participants.

Intervention

The medication adherence intervention consisted of five components: medication feedback, hypertension feedback, medication-taking skills, habit adjustment, and succinct medication and disease information delivered over an 8-week period. If the participant wished, the intervention could be conducted with spouses or the participant's adult children present, but intervention delivery was directed to the participant. The

interventionist did not provide medication education or answer questions about medications for anyone not enrolled in the study.

Baseline Education

The interventionist reviewed participants' medication regimens with each participant at the randomization visit (Time 0). The interventionist ensured the participant was able to verbalize each medication and its purpose, prescribed dosage, and frequency. Additionally, each participant was provided with a card outlining his or her medications, their purpose, dose, time to be taken, and any special instructions in clear, lay language (see Appendix D for an example). The card also included an educational graphic to help reinforce the connection between medication adherence, lower blood pressure, and positive health outcomes. The participant was instructed to keep this card in a conspicuous location near where their medications are stored (Raynor et al., 1993). In this way, the card would serve as a reminder to take the medication, and also as a quick reference of correct medication regimen information. If a participant's medication regimen changed during the course of the intervention, the medication instruction card was be updated or replaced at the next study visit to reflect the changes.

Participants also received brief education about hypertension and the health consequences of uncontrolled high blood pressure. Participants were asked questions to assess their current illness representation of hypertension such as "What do you know about high blood pressure?" and "What can be done to control your high blood pressure?" Participants then received education to reinforce knowledge about hypertension and to correct any misconceptions present in the participant's illness representation. The interventionist discussed the usual causes of hypertension, the

potential sequelae from uncontrolled hypertension, correct use of antihypertensive medications, step therapy (substituting or adding medications when BP remains elevated), and how proper adherence to antihypertensive medication may prevent the addition of unnecessary additional medications (Chobanian, Bakris, Black, Cushman, Green, Izzo, Jones, Materson, Oparil, Wright, & Roccella, 2003).

Participant education was conducted through a process of discussion. Participants were encouraged to ask questions about hypertension and their medication regimen. The interventionist answered each participant's questions to ensure that the participants' concerns and educational needs were met. In the process of answering participants' questions, the interventionist provided the structured education about hypertension and antihypertensive medication therapy.

Habit Analysis

At Time 0 intervention group participants were asked where they keep their medications. They were also asked to describe or demonstrate how their medication-taking behavior fits into their daily habits and routines. Participants were asked what habits they do each day, and whether their medication administration was (or could be) associated with another habitual behavior. If the participant did not already associate medication administration with another habitual activity, suggestions were made to guide the participant to include medication administration into daily routines (e.g., link medication-taking with toothbrushing). Visual cues were also addressed. If the participant did not have visual cues for medication administration, suggestions were provided (e.g., keep medicines next to toothbrush or near coffeepot, post brief medication instructions on medicine cabinet).

At follow-up visits, participants were asked whether they had been able to integrate medication-taking habit formation into their daily routines. If they had not, and if medication adherence remained unimproved, the interventionist would query the participant regarding what attempts the participant had made to modify daily routines to include medication administration. The interventionist assisted the participant in identifying potential new opportunities where the participant might include medication-taking in his or her daily routines.

Medication-Taking Skills

The interventionist assessed the following medication skills in each intervention group participant: 1) ability to open medication bottles; 2) ability to read medication instructions; and 3) manual dexterity for handling pills. If a participant had difficulty with any of these skills, interventions were conducted to compensate. Assistive devices were identified and implemented for opening medication bottles when necessary. Larger print on medication bottle labels, or color-coded dots on medication bottles that correspond to colors on a large-print medication instruction list were used if a participant had difficulty reading medication instructions. Finally, trays, pillboxes, or other devices for counting and sorting pills were offered as a solution for participants who have difficulty with the manual dexterity needed to extract the proper dosage from a medication bottle. Pillbox users were provided with "Tic-Tacs" to use as markers in the pillbox to remind the participant to take their antihypertensive medication from the MEMS bottle. The medication sorting trays are devices where the participant could pour multiple pills onto the tray, separate the proper number of pills to be taken, and then easily pour the rest of the pills back into the pill bottle.

Medication Adherence Feedback

Dose-Specific Feedback

At Visit 2 (Time 0), intervention group participants' MEMS caps were changed from standard MEMS TrackCaps to MEMS SmartCaps, which contain an LCD readout on the top of the cap indicating the number of times the medication bottle has been opened since midnight, and the number of hours since the last opening. This allowed participants to determine whether they had taken their daily dose(s) yet for that day. Prior research using this intervention method showed improvement in both medication adherence and blood pressure outcomes (McKenney et al., 1992).

The MEMS SmartCaps have a two-part readout on the LCD screen. The primary component is a number in the middle of the screen that displays the number of time the MEMS cap has been removed from the bottle since 12:00 a.m. that day. If the readout shows a numeral "1" the cap has been opened once since midnight. If it shows a "2" it has been opened twice, etc. The second part of the LCD readout is a series of 12 bars in a circle around the perimeter of the round LCD screen. Each bar, when showing on the screen, represents one hour since the last MEMS bottle opening. After 12 hours without any openings, a bar will begin to flash for each hour beyond 12 hours. After 24 hours without a bottle opening, all bars will flash. Opening the MEMS bottle will reset this indicator. To better facilitate the reading of the MEMS SmartCap LCD display, participants were provided with a small flashlight to store with their medication bottle.

Figure 4: *MEMS SmartCap Display*

Overall Feedback

Intervention group participants received visits every two weeks for eight weeks following randomization. At these visits, the participants' MEMS cap data was downloaded to a laptop computer. Participants were informed of their adherence level since the last visit, and were shown a graphical display of their adherence behavior to date. Similar medication adherence feedback contacts have been effective at improving medication adherence rates and lowering blood pressure (Marquez Contreras et al., 2005).

Blood Pressure Feedback

The participants' resting blood pressure was measured at each intervention visit. Participants' blood pressures were recorded on their study diaries. The interventionist

discussed the degree of change in the participants' blood pressure and how it could be positively impacted by improvements in medication adherence. Participants' blood pressures throughout the study were recorded and displayed graphically so that each intervention group participant can visualize changes in his or her blood pressure and as well as visually compare their blood pressure readings to the target blood pressure of <140/90 mmHg (<130/80 mmHg for individuals with diabetes or chronic kidney disease) recommended by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Chobanian, Bakris, Black, Cushman, Green, Izzo, Jones, Materson, Oparil, Wright, & Roccella, 2003).

If a participant's blood pressure was well controlled (at or below the JNC-7 goal) despite low medication adherence, the participant was queried as to whether he or she had been using the MEMS bottle and cap when taking his or her antihypertensive medication. If the participant admitted to not using the MEMS cap, the participant was reminded of the importance of using the MEMS cap for measuring study outcomes. The investigator explained to the participant that if they chose not to use the cap, information from their participation would not be usable and they would be withdrawn from the study. If the participant stated that he or she had been using the MEMS cap and believed that their MEMS data reflected his or her medication-taking behavior, then the participant was advised to discuss their current medication regimen with their prescribing care provider. In such a situation, the participant could be a candidate for lowering the antihypertensive medication dosage or eliminating an antihypertensive medication.

If a participant's blood pressure remained high, but MEMS data indicated good adherence, the participant was counseled to discuss with his or her prescribing care

provider the possibility of moving to the next step of therapy to try to better control the participant's blood pressure.

Control Group

The control group for this study received usual care. After randomization, control group participants were seen by the investigator only for data collection (See Figure 4). Medication education was conducted only to the extent necessary to address medication safety concerns identified by the investigator. An alternative control method would be to develop an attention-control group, but such a method was beyond the resources of this exploratory study. Future research with this intervention protocol will involve the development of an attention-control study arm. In this study, control group participants were provided with educational materials on arthritis pain ("Arthritis Answers" from the Arthritis Foundation).

Study Procedures

Recruitment

Participants were recruited from locations in the Columbia, Missouri and St. Louis, Missouri metropolitan areas. Recruitment occurred through word-of-mouth and via flyers posted in public locations including, but not limited to, churches, senior centers, and grocery stores. The principal investigator also provided information about the study to several physicians (geriatricians and other primary care providers with large older adult patient populations), community health nurses, and parish nurses in the St. Louis area, requesting that they refer older patients they thought may be having difficulty with adherence to their antihypertensive medication regimen. Finally, the principal

investigator contacted and made brief presentations at senior centers and church senior citizen groups about the study.

When a potential participant expressed interest in the study, she or he was contacted by phone and provided additional information about the study. During this phone contact, potential participants were screened for initial eligibility to ensure that they were: 1) over 60 years of age; and 2) currently taking at least one medication for hypertension. If the potential participant remained interested and met the screening criteria, an initial study visit was scheduled. If the potential participant wished to review the consent form prior to the initial study visit, a copy of the consent form was provided to the participant. If the potential participant declined to review the consent form prior to the study visit, he or she was provided any time necessary to review the consent at the first study visit prior to the informed consent discussion with the principal investigator.

Study Visits

Study participation involved three visits for participants in the control group and seven visits for those in the intervention group. An outline of study procedures for each visit is shown in Table 5.

Table 5: *Outline of Study Procedures*

Visit	1	Phone call	2	2A	2B	2C	2D	3
Week	-6	-5	0	2	4	6	8	12
Informed Consent	X							
Collect Demographic Information	X							
Medical History	X							
Record/Update Medication Regimen	X		X	X[1]	X[1]	X[1]	X[1]	X
SPMSQ	X							
BMQ	X							X
Initiate MEMS use & provide diary	X							
Phone contact to assess MEMS use		X						
Randomization			X					
Record Blood Pressure	X		X	X[1]	X[1]	X[1]	X[1]	X
Download MEMS data			X	X[1]	X[1]	X[1]	X[1]	X
Provide Baseline Education			X[1]					
Habit Analysis			X[1]	X[1]	X[1]	X[1]	X[1]	
Medication-taking skills training			X[1]					
Provide Adherence & BP Feedback			X[1]	X[1]	X[1]	X[1]	X[1]	
Collect and review diary card								X

Note: Visits 2A, 2B, 2C, and 2D are for intervention group only.
[1]Intervention group only.

Visit 1: Screening

At the initial visit, the investigator again reviewed the study procedures, risks, and benefits with the participant. Participants were encouraged to ask any questions they may have about the study. As part of this informed consent process, the participant and investigator signed the informed consent document, and a signed copy was provided to the participant. The consent process took place prior to any other study procedures.

Once informed consent was obtained, the participant was further screened for study eligibility. Demographic information was collected, a brief self-reported medical history was taken (list of current diagnoses), and information was collected on all

medications being taken at the time of study enrollment. The SPMSQ was then administered. If the participant remained eligible, participants completed the BMQ. Then blood pressure was measured and a MEMS TrackCap was installed on one of the participant's antihypertensive medication bottles. If the participant was taking more than one antihypertensive medication, the MEMS cap was placed on the medication with the greater number of daily doses. Participants were instructed on the use of MEMS caps, and were provided with a diary for recording any accidental or extra medication bottle openings. A follow-up visit was scheduled to occur at least six weeks from the screening visit.

Phone Contact: Screening

One week after Visit 1, the investigator contacted each participant by telephone to assess MEMS cap use and answer questions or solve problems the participant may have had regarding the MEMS. The questions asked during this telephone call are found in the appendix. This approach has been successful in improving use of MEMS caps in other medication adherence studies (C. Russell, personal communication, May 15, 2008).

Visit 2: Randomization

Screening. At the second visit, MEMS cap data were downloaded to a laptop computer. Any accidental or extra openings recorded on the participant's diary were noted. If the participant's adherence level for the last two weeks was greater than 85%, the MEMS cap was collected and the participant was thanked for their time. If the adherence level was less than 85%, the participant's blood pressure was measured and the participant was randomized to either the intervention or control groups.

Randomization. At this point, participants were assigned a subject number based on the order of enrollment and randomized to the intervention or control groups. Randomization was conducted via an envelope method, where the group allocation was assigned by computerized randomization software, and each subject number's group assignment had been placed in a sealed, numbered envelope by someone other than the principal investigator. The treatment and control groups were allocated in a 2:1 ratio, with ten participants in the treatment group and five participants in the control group.

Following randomization, participants in the control group scheduled another study visit for approximately 12 weeks from Visit 2. This concluded the visit for control group participants. Intervention group participants then received the intervention (baseline education, habit analysis, and feedback). Visits were scheduled with intervention group participants for 2, 4, 6, and 8 weeks after randomization.

Intervention Visits

Intervention group participants were visited bi-weekly for monitoring of medication adherence and blood pressure. Participants were informed of their medication adherence rates and their blood pressure verbally and also on a graphical display to provide feedback on their level of adherence and blood pressure control. Participants were asked if any changes had been made to their prescribed medication regimen. Any medication changes were recorded, and the written medication instructions were updated.

Visit 3: Outcomes

Visit 3 was conducted for all participants and occurred approximately twelve weeks after Visit 2. Any changes to participants' health status and/or medication regimen were recorded. Participants were asked to complete the BMQ. MEMS diary cards were

then reviewed and collected. Blood pressure was measured. Participants were thanked for their generous participation in the research study. Visit 3 was the final data collection point for this study. Due to its exploratory nature, it was beyond the scope of this project to examine persisting behavior change.

Final visit feedback. At the final study visit, all participants (intervention and control) received medication adherence and blood pressure feedback. Control group participants were offered the medication education, habit analysis, and medication skills assessment provided to intervention group participants at Visit 2. If a participant's adherence level was very low but blood pressure remained high, the participant was counseled regarding the need to better adhere to his or her antihypertensive medication. Participants with very poor medication adherence but a blood pressure below their JNC-7 target were advised to discuss with their primary health care provider the possibility of scaling back their antihypertensive medication regimen. Finally, if a participant's MEMS data demonstrated good adherence but his or her blood pressure remained high, a recommendation was made to the participant to discuss with his or her primary health care provider the possibility of modifying the participant's antihypertensive dose or medication choice to attempt to achieve better blood pressure control.

Assessment of Study Feasibility

At the final study visit, participants were asked to provide feedback based on their experience in the study. Specifically, they were asked whether they found participation in the study to be burdensome, and what they would prefer to have been conducted differently. Intervention group participants were asked whether they found the MEMS SmartCaps useful, and whether they felt the medication adherence intervention was

helpful to them. They were also asked their opinion on the length and intensity of the intervention program, and whether they had any suggestions for improvement. The investigator recorded this information using extensive field notes.

Intervention Blinding and Safety

Maintenance of Intervention Integrity

The nature of this health behavior intervention prevented the study from being blinded, as participants were aware that they were receiving the study intervention. Steps were taken, however, to minimize the potential for contamination between treatment and control groups. No two individuals from the same household were enrolled in the study. Control group participants asking about their adherence level were informed that that information could not be disclosed to them until they completed the study. If control group participants asked about their hypertension medications, they were referred back to their primary care provider or pharmacist for any information that could not be obtained from the medication label or pharmacy packaging.

Medications Other Than Antihypertensive Medications

If participants had questions about medications other than antihypertensive medications, the investigator clarified information about the purpose, and administration instructions (dose, frequency, timing, etc.) but deferred questions involving concerns about side effects, medication choice, or appropriateness to the participant's primary care provider or pharmacist.

Inappropriate medications. As a safety measure, participants' medications were reviewed using the 2002 revision of the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (Beers, 1997; Fick et al., 2003). Participants found to

have prescriptions for multiple medications at a high Beers Criteria severity rating, or a medication prescribed or being taken at a dangerous dosage or frequency, were informed of the potentially harmful situation. Participants with inappropriate medications were strongly encouraged to address the situation with their primary care provider as soon as possible.

Acute Health and Well-Being Concerns During Study Visits

If, during a study visit, a participant was found to be experiencing symptoms of acute distress (e.g., myocardial infarction, respiratory distress, stroke) the participant was assessed and steps taken to assist the participant in contacting the participant's family, primary care provider, and/or emergency medical personnel as needed.

If the investigator discovered signs that study participants were experiencing elder abuse or neglect, a report would be made to the Missouri Department of Health and Senior Services Elder Abuse and Neglect Hotline.

Reasons for Study Withdrawal

A participant would have been withdrawn from the study if all of his or her antihypertensive medications were discontinued during the course of the study. Participants would also be withdrawn from the study if, during the study, they became no longer responsible for managing and administering their own medications (except for brief hospitalizations where the participant resumes self-medication following discharge). Finally, participants may have been withdrawn from the study if, in the investigator's judgment, the participant's health condition or situation had changed such that study participation now posed a risk to the participant's health or well-being.

Data Management and Analysis

All study records were stored in a locked file cabinet in the investigator's office area. Study data was entered into a computerized spreadsheet and imported into the Statistical Package for the Social Sciences 13.0 (SPSS Inc., Chicago, IL). Descriptive statistics were calculated for all measures.

Research Question 1: Adherence

Medication adherence was calculated as the percentage of antihypertensive medication doses taken within prescribed intervals. This method prevents the missing of a dose on one day from being negated by taking an extra dose on another day. It also takes into account the timing of doses in relation to one another. Extra openings for medication refills or accidental openings recorded on participants' diary cards were excluded from adherence rate calculation. Periods of hospitalization were also excluded from adherence rate calculation.

Graphs of medication adherence rates were constructed using group means and standard deviations at both baseline and week 12 to compare group effects. Scatterplot graphs were also constructed to examine data for outliers. Effect sizes were calculated for suggesting the required sample size for subsequent studies.

Research Question 2: Blood Pressure

Data analysis was conducted by graphing resting systolic and diastolic blood pressure for the treatment and control groups at both baseline and week 12. Graphs were constructed using the group means and standard deviations to compare group effects. Scatterplot graphs were also constructed to examine data for outliers. Effect sizes have been calculated for blood pressure outcomes.

Research Question 3: Study Recruitment

Study enrollment rates were calculated by tracking the number of persons interested in the study, the number screened for enrollment, and the reasons for study exclusion for any participants excluded from study participation. The number of individuals randomized were divided by the number screened to determine the enrollment rate. Reasons for ineligibility or participants' decision not to participate were tracked, along with rates and reasons for any participants who dropped out or were withdrawn from the study. The number of participants recruited and screened was divided by the number of participants who completed the study to determine a ratio to guide future study recruitment. This may differ from the enrollment rate if any participants failed to complete the study.

Research Question 4: Visit Duration

The beginning and end time of each study visit was recorded. The mean, standard deviation, and range for the duration of each visit was calculated.

Research Question 5: Study Feasibility

Participants' responses to questions about their study participation and intervention experience was evaluated for themes. All feasibility data—enrollment rates, reasons for study exclusion, visit duration, and participant evaluations will be used to refine the intervention protocol and in the design of follow-up trials.

CHAPTER FOUR: RESULTS

The purpose of this exploratory study was to test whether a feedback-based adherence intervention improved medication adherence among a sample of community-dwelling older adults with hypertension. A secondary aim was to evaluate whether the intervention had any effect on resting blood pressure levels.

Sample Demographics

A total of 33 participants completed the study screening period. Fifteen participants were eligible to be randomized into the study, 10 in the treatment group and 5 in the control group. There were no statistically significant differences between intervention and control groups at baseline. The randomized sample was 73% female and 60% Caucasian (see Table 6). Participants' age ranged from 60 to 87 years, with a mean of 72.47 (see Table 7). Participants' estimates of their number of years with hypertension ranged from 5 to 50 years. The participants took an average of 5.8 daily prescription medications and 2.93 over-the-counter medications per day.

Table 6: *Sample Demographics for Frequencies*

Variable	Intervention Group (n=10)	Control Group (n=5)	Total Sample (n=15)
Gender (% Female)	80%	60%	73%
Race			
Caucasian	60%	60%	60%
African-American	30%	40%	33%
Hawaiian/Pacific Islander	10%	0%	7%

Table 7: *Sample Demographics for Continuous Variables*

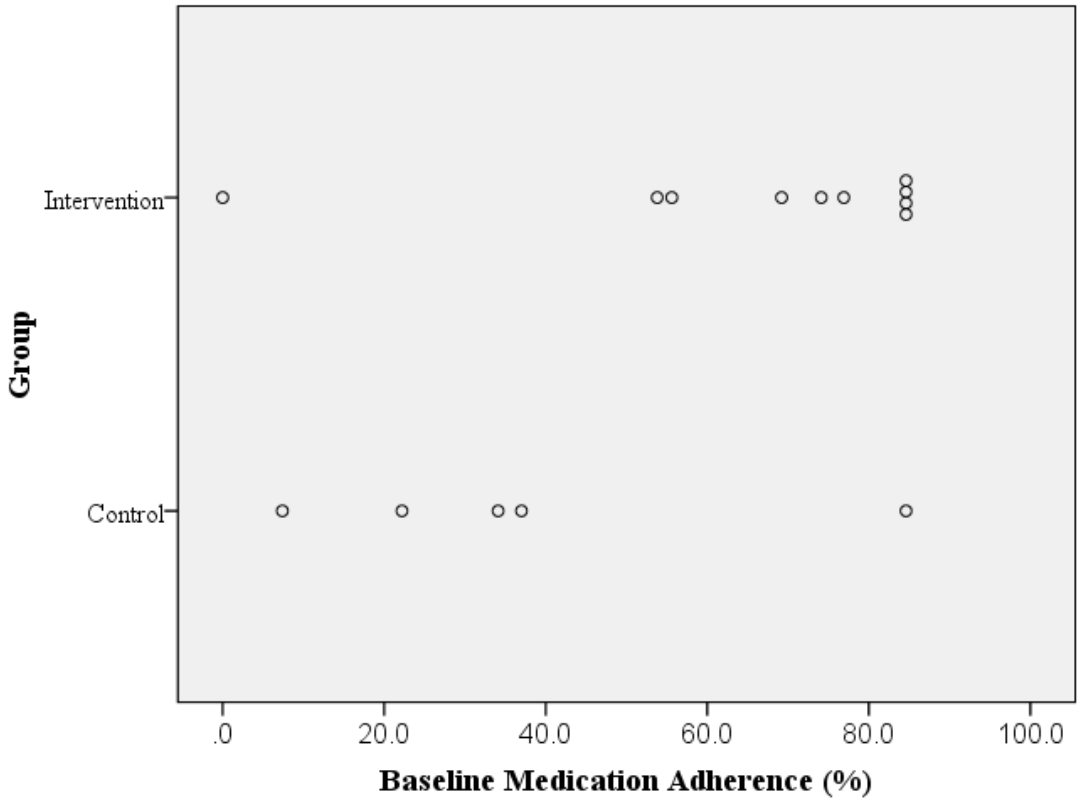
Variable	Intervention Group (n = 10) mean (*SD*)	Control Group (n = 5) mean (*SD*)	Total Sample (n = 15) mean (*SD*)	*t*	*p*
Age	73.70 (9.30)	70.00 (6.96)	72.47 (8.53)	-.781	.449
Years with HTN	17.90 (13.27)	17.60 (16.70)	17.80 (13.89)	-.038	.970
Number of Daily Prescription Medications	5.60 (2.55)	6.20 (3.96)	5.80 (2.96)	.308	.769
Number of Daily OTC Medications	3.50 (2.72)	1.80 (2.68)	2.93 (2.74)	-1.146	.272
SPMSQ Score	1.10 (0.74)	1.00 (0.71)	1.07 (0.70)	-.251	.806
Baseline Adherence Rate (%)	66.80 (26.22)	37.06 (29.02)	56.89 (29.88)	-2.003	.066
SBP (mmHg)	136.00 (19.21)	151.20 (17.58)	141.07 (19.51)	1.482	.162
DBP (mmHg)	74.40 (10.70)	82.40 (17.40)	77.07 (13.24)	1.112	.286

Note: SD = Standard Deviation; HTN = Hypertension; OTC = over-the-counter; SPMSQ = Short Portable Mental Status Questionnaire; SBP = systolic blood pressure; DBP = diastolic blood pressure

Baseline Measures

Baseline medication adherence across the sample ranged from 0% to 84.6%, with a mean of 56.9% (*SD* = 29.88). The mean medication adherence rate in the control group was lower than the mean rate in the intervention group (see Table 7). The difference between groups was not statistically significant (t = -2.003, p = .066). A scatterplot of baseline medication adherence rates for each group is shown in Figure 5.

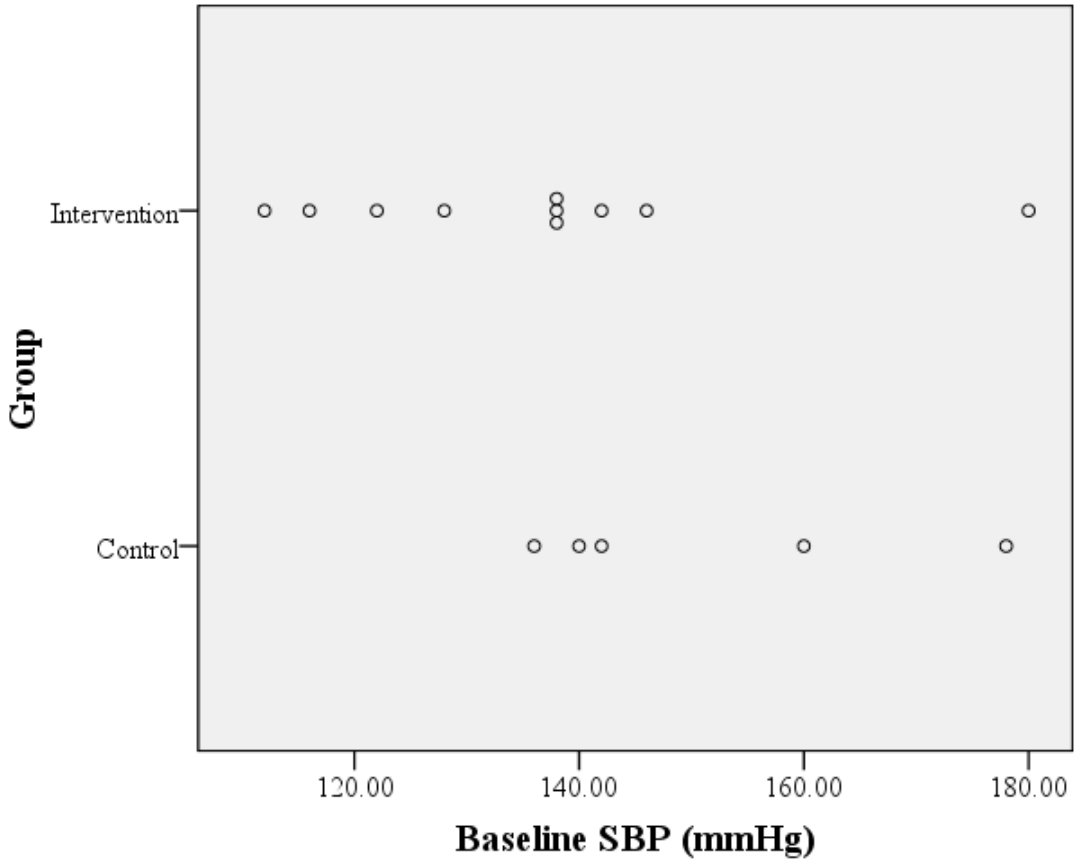
Figure 5: *Baseline Medication Adherence*



Resting systolic blood pressure (SBP) at baseline ranged from 112 mmHg to 180 mmHg, with a mean of 141.07 mmHg (*SD* = 19.51). The intervention group's baseline

resting SBP ranged from 112 mmHg to 180 mmHg, with a mean of 136.0 mmHg (*SD* = 19.21). The control group's baseline resting SBP ranged from 136 mmHg to 178 mmHg, with a mean of 151.2 mmHg (*SD* = 17.58). The difference between groups was not statistically significant ($t = 1.482$, $p = .162$).

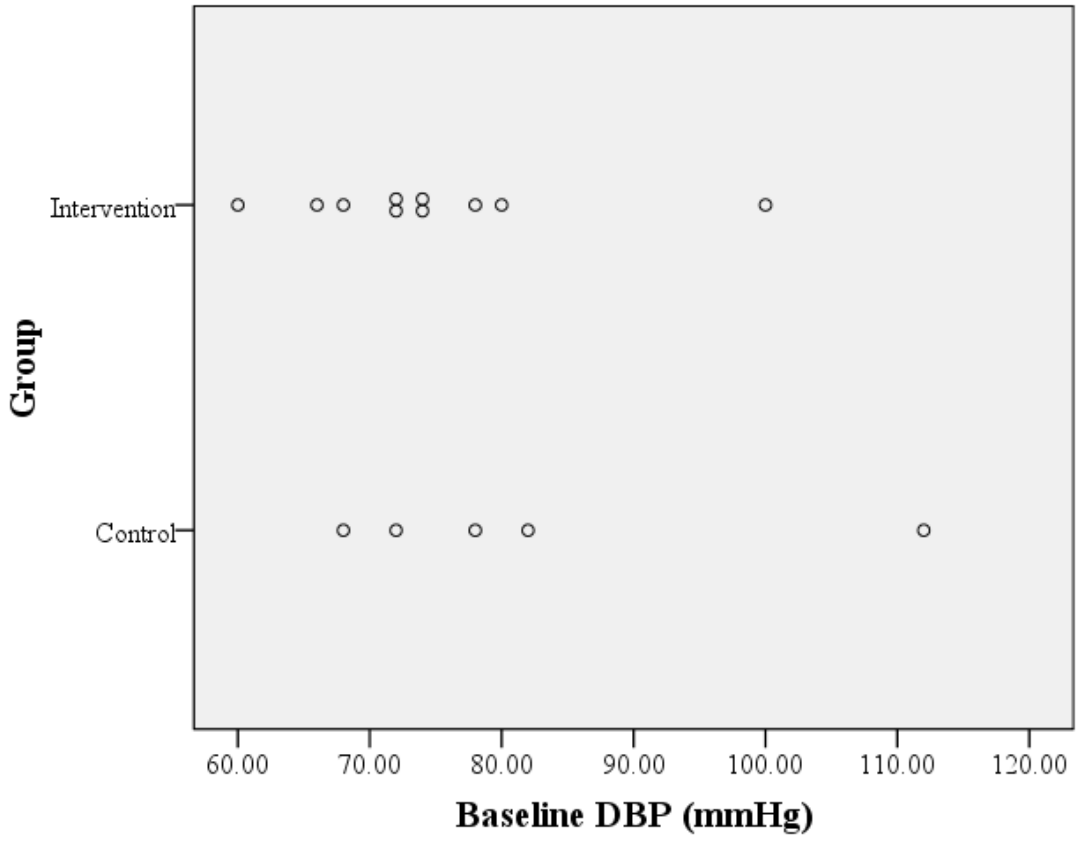
Figure 6: *Baseline Systolic Blood Pressure*



Resting diastolic blood pressure (DBP) at baseline ranged from 60 mmHg to 112 mmHg, with a mean of 77.07 mmHg (*SD* = 13.24). The intervention group's baseline resting DBP ranged from 60 mmHg to 100 mmHg, with a mean SBP of 74.4 mmHg (*SD* = 10.70). The control group's baseline resting DBP ranged from 68 mmHg to 112 mmHg

with a mean DBP of 82.4 mmHg (*SD* = 17.40). The difference between groups was not statistically significant (*t* = 1.112, *p* = .286).

Figure 7: *Baseline Diastolic Blood Pressure*



Primary Outcome Measures

Research Question 1: Medication Adherence

Research Question 1: Were medication adherence rates in older adults with hypertension who received a feedback-based medication adherence intervention higher than those who received no intervention?

Adherence rates before and after intervention are presented in Table 8. The mean adherence rate improved among intervention group participants over the course of the 8-week intervention program. At 12-weeks post-randomization, the mean adherence score for the intervention group was 81.14%, a mean improvement of 12.80%. The control group participants experienced a slight worsening in adherence from randomization to week 12, from 37.06% to 36.00%.

Table 8: *Medication Adherence Change*

Variable	Intervention Group (n = 10) mean (*SD*)	Control Group (n = 5) mean (*SD*)	*t*	*p*
Baseline Adherence	66.80 (26.22)	37.06 (29.02)	-2.003	.066
12-Week Adherence	81.14 (33.26)	36.00 (37.71)	-2.376	.034
Mean Adherence Change	12.80 (13.78)	-1.06 (15.59)	-1.762	.102

The medication adherence change score effect size (Cohen's *d*) was 1.35. This represents a large effect from the intervention.

Research Question 2: Resting Blood Pressure

Research Question 2: Was resting blood pressure among older adults with hypertension who received a feedback-based medication adherence intervention lower than those who received no intervention?

The mean systolic blood pressure (SBP) in the intervention group decreased from 136.00 (*SD* = 19.21) to 132.20 (*SD* = 12.45) at 12-weeks post-randomization. The mean systolic blood pressure in the control group changed from a baseline of 151.20 (*SD* =

17.58) to 170.00 (*SD* = 44.25) at 12 weeks (see Table 9). Mean SBP change scores were –2.40 (*SD* = 18.25) for the intervention group and 18.80 (*SD* = 31.20) for the control group.

Table 9: *Blood Pressure Change*

Variable	Intervention Group (n = 10) mean (*SD*)	Control Group (n = 5) mean (*SD*)	*t*	*p*
Baseline SBP	136.00 (19.21)	151.20 (17.58)	1.482	.162
12-Week SBP	132.20 (12.45)	170.00 (44.25)	1.873	.129
Mean SBP Change Score	-2.40 (18.25)	18.80 (31.20)	1.681	.117
Baseline DBP	74.40 (10.70)	82.40 (17.40)	1.112	.286
12-Week DBP	74.40 (10.53)	92.00 (19.34)	2.320	.037
Mean DBP Change Score	-0.40 (8.88)	9.60 (8.65)	1.906	.079

Note. SBP = systolic blood pressure; DBP = diastolic blood pressure; SD = standard deviation

Mean diastolic blood pressure (DBP) was essentially unchanged from 74.40 (*SD* = 10.70) to 74.40 (*SD* = 9.97) in the intervention group from baseline to 12-weeks, respectively. In the control group, DBP changed from 82.4 (*SD* = 17.40) at baseline to 92.00 (*SD* = 19.34) at 12 weeks post-randomization. Mean DBP change scores were 0.40 (*SD* = 8.88) in the intervention group and 9.60 (*SD* = 8.65) in the control group.

The effect sizes (Cohen's *d*) for blood pressure change scores were 0.99 for SBP and 1.12 for DBP.

Secondary Outcome Measures

Research Question 3: Recruitment

Research Question 3: How many participants were necessary to recruit and assess to identify 15 older adults with <85% adherence?

A total of 33 participants completed screening to identify the 15 eligible volunteers for this study. This translates to a 45.5% eligibility rate. Some potential participants who expressed interest in the study self-excluded or reversed their decision about participation prior to their screening visit. No study volunteers who completed screening withdrew from the study. Seventeen were excluded based on medication adherence during screening. One participant was excluded due to a change in health status during the screening period that left her no longer self-administering her own medications.

Demographic differences between eligible and excluded participants are shown in Table 10. The excluded participants had a larger proportion of women to men than did the eligible participants. There were also fewer African-Americans and more Caucasians in the excluded sample.

Table 10: *Demographic Differences Between Eligible and Excluded Participants*

Variable	Eligible (n=15)	Excluded (n=18)
Gender (% Female)	73%	83%
Race		
Caucasian	60%	94%
African-American	33%	6%
Hawaiian/Pacific Islander	7%	0%

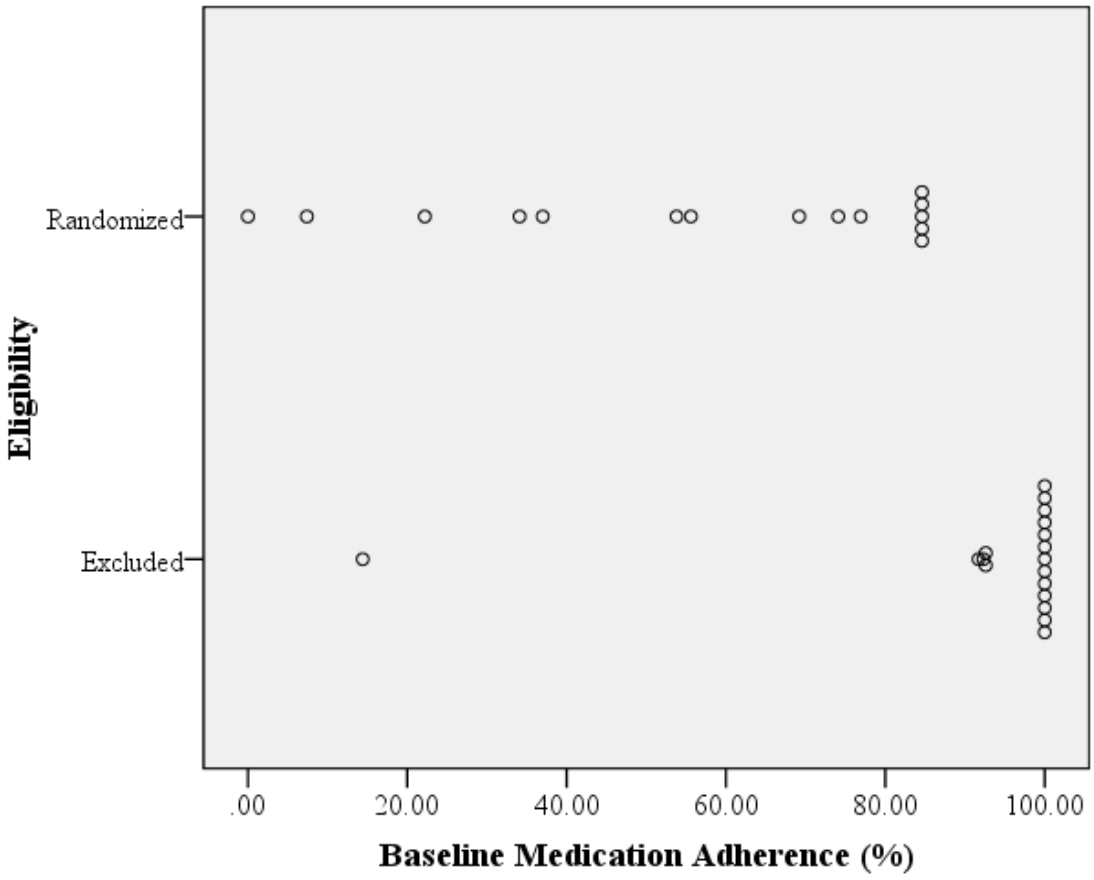
For continuous variable baseline screening measurements, only the baseline medication adherence rate was significantly different (see Table 11). Eligible participants had a mean adherence rate of 56.89%, while those excluded from the study had a mean adherence rate of 93.53% ($t = 4.052$, $p < .001$). The distribution of medication adherence rates for randomized and excluded participants is shown in Figure 8.

Table 11: *Baseline Differences Between Eligible and Excluded Participants*

Variable	Eligible (n = 10) mean (*SD*)		Excluded (n = 5) mean (*SD*)		*t*	*p*
Age	72.47	(8.53)	76.39	(6.41)	1.508	.142
Years with HTN	17.80	(13.89)	14.10	(11.99)	-0.822	.417
Number of Daily Prescription Medications	5.80	(2.96)	4.33	(1.97)	-1.641	.114
Number of Daily OTC Medications	2.93	(2.74)	2.33	(1.91)	-0.740	.465
SPMSQ Score	1.07	(0.70)	1.28	(0.75)	0.827	.415
Baseline Adherence Rate (%)	56.89	(29.88)	93.53	(20.02)	4.052	<.001
SBP (mmHg)	141.07	(19.51)	147.22	(16.44)	0.984	.333
DBP (mmHg)	77.07	(13.24)	76.00	(7.06)	-0.296	.770

Note: SD = Standard Deviation; HTN = Hypertension; OTC = over-the-counter; SPMSQ = Short Portable Mental Status Questionnaire; SBP = systolic blood pressure; DBP = diastolic blood pressure

Figure 8: *Baseline Medication Adherence by Eligibility Status*



Research Question 4: Study Visit Time

Research Question 4: How much time did the intervention visits require?

Initial screening visits lasted from 28 to 80 minutes, with an average visit duration of 45 minutes (*SD* = 12). Second visits ranged from 8 to 58 minutes, with an average visit duration of 24 minutes (*SD* = 13). Second visits were significantly longer for eligible participants versus ineligible participants, with mean visit durations of 33 minutes and 17 minutes, respectively ($p = .001$). Bi-weekly feedback visits for intervention group participants ranged from 10 to 35 minutes in length, with a mean duration of 15 minutes (*SD* = 4).

Research Question 5: Participant Feedback

Research Question 5: Did study participants report any problems or unexpected burden from study participation?

At Visit 3, each participant was asked about his or her experience in the study. No participants reported feeling the study was burdensome. Several intervention group participants reported that they felt the MEMS SmartCap was helpful to them in improving their medication adherence. Many participants found that seeing their medication adherence pattern on the computer screen during the feedback visits helped them to see what their medication-taking patterns were and to make adjustments as needed. One participant in particular verbalized using the adherence feedback as a way to work toward a personal medication adherence goal.

CHAPTER FIVE: DISCUSSION

The purpose of this exploratory study was to test whether a feedback-based adherence intervention improved medication adherence for community-dwelling older adults with hypertension. A secondary purpose was to evaluate whether the intervention had any effect on resting blood pressure levels. This chapter discusses the results of the study in relation to the study aims, existing literature, and conceptual framework. It will also address the study's strengths and limitations as well as implications for clinical practice and future research.

Medication Adherence Findings

It is difficult to compare improvement in medication adherence across studies due to the differences in adherence measurement methods employed in much of the medication adherence literature. Participants receiving the intervention in this study saw a mean improvement in adherence of 12.80%, which is a larger improvement than in other medication adherence interventions using adherence feedback as an intervention component (Chabot et al., 2003; Marquez Contreras et al., 2005). This may be due to the fact that this study focused on persons who were nonadherent at baseline, and possibly that the intervention was delivered face-to-face, rather than by telephone, and provided objective visual feedback from the MEMS caps.

The effect size of 1.40 is larger than the effect size of 0.33 for medication adherence outcomes found in a recent meta-analysis of medication adherence interventions for older adults (Conn et al., in press) and is larger than the medication adherence effect sizes found in earlier meta-analyses (Devine & Reifschneider, 1995; Peterson, Takiya, & Finley, 2003). The meta-analysis by Conn and colleagues (in press)

included randomized controlled trials of medication adherence interventions in older adults for all types of health conditions, and was not limited to interventions focusing specifically on medication adherence. Peterson and colleagues' (2003) meta-analysis looked at medication adherence interventions tested in all age groups, and found a very small effect size of $r = 0.08$. Using the formula from Friedman (1968), this is equivalent to a Cohen's d of 0.16. Finally, an older meta-analysis by Devine and Reifschneider (1995) focused on interventions to improve hypertension outcomes, and found a medication adherence effect size of $d = 0.74$ across 17 studies. The results of this current exploratory RCT are somewhat consistent with Devine and Reifschneider's synthesis, except that the while the adherence effect sizes in the meta-analysis were large, the blood pressure effect sizes were much smaller than what has been found in this study.

The medication adherence rates, both pre- and post-intervention in this study were consistent with or better than those found in other antihypertensive medication adherence studies using MEMS technology where adherence was determined using dosing intervals (de Bruin, Hospers, van den Borne, Kok, & Prins, 2005; Rosen, Rigsby, Salahi, Ryan, & Cramer, 2004; Schmitz, Sayre, Stotts, Rothfleisch, & Mooney, 2005) but lower than studies measuring adherence using less stringent methods of calculating adherence, such as the correct number of doses per day (Santschi, Rodondi, Bugnon, & Burnier, 2008; Vrijens, Belmans, Matthys, de Klerk, & Lesaffre, 2006). Unfortunately, much of the previous research has only addressed the number of doses consumed instead of considering the timing of doses. Such differences in operational definition make it difficult to compare intervention effectiveness.

Differences between adherence outcomes in this study and others using MEMS may also be due in part to the fact that this study excluded individuals who were already adherent with their antihypertensive medications. Many medication adherence studies do not restrict enrollment to those who are nonadherent at baseline. Evidence also suggests that individuals continuing an established antihypertensive medication have lower and more variable adherence than those beginning a new medication (Kruse, Rampmaier, Ullrich, & Weber, 1994). This study's focus on individuals on established antihypertensive therapy would lead to an expectation of lower, more inconsistent medication adherence rates.

Blood Pressure Findings

Blood pressure outcomes from antihypertensive medication adherence interventions are widely varied, and demonstrate that not all adherence interventions have an effect on clinical outcomes (Bertholet, Favrat, Fallab-Stubi, Brunner, & Burnier, 2000; de Castro et al., 2006; Devine & Reifschneider, 1995; Friedman et al., 1996; Girvin et al., 1999; Hunt et al., 2004; Marquez Contreras et al., 2005; Santschi et al., 2008; Vivian, 2002; Wetzels et al., 2007). The 0.99 effect size for systolic blood pressure outcomes was larger than that found in a recent meta-analysis of medication adherence interventions for older adults, where the effect size for SBP outcomes across eight studies was 0.21 (Conn et al., in press). The diastolic blood pressure effect size was also larger than the effect size for DBP found in the meta-analysis (Conn et al., in press). It is possible that studies in the meta-analysis which reported BP may not have been limited to patients with hypertension. This would have limited the blood pressure improvement in those studies. There may also have been differences in the degree if initial BP severity between the

study samples that would impact the ability to detect improvement in blood pressure outcomes.

The changes in blood pressure along with the improved medication adherence outcomes are promising, but should be interpreted with caution. It is difficult to relate blood pressure outcomes directly to changes in adherence due to the presence of other confounding variables. Blood pressure is impacted by other factors such as medication choice, diet, exercise, and the possibility of refractory hypertension. Additionally, linking adherence to blood pressure outcomes is not appropriate in very small sample studies where other variables can not be well controlled.

Feasibility

The intervention was able to be effectively delivered to the study participants without any report of undue burden to the participants. Most participants reported a sense of benefit from the intervention, particularly from the feedback components. The intervention was designed to provide an intervention dose that would be adequate, but not burdensome. Short-term interventions of one week or less and long-term interventions of several months tend to be less effective than interventions lasting several weeks (Conn et al., in press).

The primary benefit of the intervention was from the adherence and blood pressure feedback. Intervention group participants looked forward to receiving information about their adherence level and blood pressure control. Many intervention participants would compare their adherence and blood pressure levels to those from their prior visit to gauge their progress and the need for further attention to their medication-taking behavior.

The habit analysis was helpful in only a few cases. Most intervention group participants reported at the first intervention visit that their medication-taking behavior was already integrated into their daily habits and routines. In some cases, however, MEMS data at feedback visits allowed the interventionist to analyze participants' dosing times and suggest modifications to daily routines to facilitate improved adherence by changing medication administration times, or by linking medication administration do a different routine behavior. While the habit analysis component of the intervention may not have been applicable to all study participants, it was of benefit to those who did not have their medication-taking behavior linked to other daily habits or routines. As it was not perceived as burdensome to those who did not need it, it should remain as part of the intervention protocol.

Conceptual Framework

While the study did not include measures for each of the components in the theoretical framework, the study findings support the use of a model that incorporates cognitive factors of medication-taking behavior but focuses on behavioral approaches to medication adherence behavior change. The incorporation of behavioral, cognitive, and environmental factors is important to adequately address the multifaceted nature of medication adherence. This study showed that an intervention incorporating medication adherence and blood pressure feedback had an effect on medication adherence. The exact mechanism of action of the intervention is not yet known. Additional study is needed to better analyze the relationships between the constructs found in the conceptual framework.

Strengths and Limitations

Several methodological features contributed to the strength of this study. This study had a robust randomized controlled trial design, which allows the comparison of outcomes between separate intervention and control groups. Unlike much of the prior literature in this area, this study focused exclusively on older adults who were in the maintenance phase of their antihypertensive medication. This prevented confounding from the differences in medication adherence found between those who are just beginning a new medication regimen and those who have been taking the regimen for some time. This study's focus on individuals with adherence problems at baseline was another strength, in that it prevented ceiling effect and evaluated the effectiveness of the intervention in the population of people who would be in need of adherence improvement in clinical practice.

A primary limitation of this study is its scope. As an exploratory study, the small sample size and resulting lack of statistical power prevents analysis of the results for statistically significant effects from the intervention, limiting the interpretation of findings. The study is also limited in that the blood pressure outcome measure only measures a single point in time, and can be affected by several outside factors (e.g., time of day, length of time since last antihypertensive medication dose, etc.). Future research would be improved by using 24-hour ambulatory blood pressure monitoring.

The study also does not adequately control for differences in antihypertensive therapy, and cannot account for the possibility that a study participant may not be on the proper antihypertensive drug, and that their regimen may not be following the JNC-7 guidelines. It is also impossible in this type of study to account for individuals who may

have refractory hypertension that simply does not respond to conventional medication therapy.

The ability to link study outcomes to the conceptual framework is also limited in this study. Future work will need to include measures of additional concepts represented in the study (e.g., illness interpretations, medication beliefs, barriers to obtaining medications). Such measures would better permit explanation of the effect of the intervention and a better analysis of factors contributing to variance in medication adherence outcomes.

Implications for Clinical Practice

The results of this study indicate that an advanced practice nurse-delivered behavioral feedback approach to improving medication adherence may be effective for older adults taking medication for hypertension. Providing verbal and visual feedback on adherence levels, linked with resting blood pressure readings, can facilitate changes in daily habits and routines to improve medication adherence and, as a result, blood pressure control.

Implications for Future Research

This study indicates that the tested intervention has an adequate effect size to warrant further testing in a larger randomized controlled trial. Additional research is needed to determine specifically how the adherence and blood pressure feedback influences medication-taking behavior, and whether such interventions also modify medication beliefs and illness interpretations. The role of environmental and system factors on medication adherence continues to need further study.

Further research must also address issues with patterns of adherence, and how expected variations in daily routines impact medication adherence. It is unknown whether such variations, such as taking medications several hours early two mornings each week, create a negative clinical effect. Additionally, future work should address the effect of the intervention on other populations, such as those with cognitive deficits, those just beginning new antihypertensive therapy, and those who have assistance in managing their medications.

Conclusion

This study demonstrates the potential effectiveness of this feedback-based antihypertensive medication adherence intervention protocol for older adults. The moderate to large effect sizes for medication adherence and blood pressure outcomes indicate the benefit of expanded testing to determine intervention effectiveness.

The feasibility evaluation has shown the intervention protocol to be well-received by the older adult participants, who did not view the study as burdensome or disruptive to their lives, but rather saw it as a benefit and an aid to their medication adherence and blood pressure control.

Future research will require a design and sample size with adequate power for tests of statistical significance and the ability to analyze for subgroup differences due to variables such as number of medications, number of daily doses, baseline adherence rate, and antihypertensive medication class.

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APPENDIX A: Commonly-Used Antihypertensive Medications

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)

APPENDIX B: SPMSQ Exam

Short Portable Mental Status Questionnaire

Instructions: Ask questions 1-10 in this list and record all answers. Ask question 4A only if participant does not have a telephone. Record the total number of errors based on the ten questions.

1. What is the date today? _____ _____ _____
   Month Day Year
2. What day of the week is it? _____
3. What is the name of this place? _____
4. What is your telephone number? _____

4A. What is your address? (ask only if participant has no telephone) _____

_____

5. How old are you? _____
6. When were you born? _____
7. Who is the President of the United States now?

   _____
8. Who was President just before him?

   _____
9. What was your mother's maiden name?

   _____
10. Subtract 3 from 20 and keep subtracting from each new number, all the way down.

    17 14 11 8 5 2

Comments: _____

_____

Score: _____ 0 – 2 errors: Intact intellectual functioning
3 – 4 errors: Mild intellectual impairment
5 -7 errors: Moderate intellectual impairment
8 – 10 errors: Severe intellectual impairment

Scoring Guidelines:

All answers must be given by the participant without reference to calendar, newspaper, birth certificate, or another memory aid.

Question 1: Scored as correct only when the exact month, exact date, and exact year are given correctly.
Question 2: Must give correct day of the week.
Question 3: Should be scored as correct if any correct description of the location is given. "My home," correct name of the town or city of residence, the name of the facility or institution, are all acceptable.
Question 4: Should be scored as correct when the correct telephone number can be verified, or when the participant can repeat the same number at another point in the questioning.
Question 5: Should be scored as correct when stated age corresponds to the date of birth.
Question 6: Is to be scored as correct only when the month, exact date, and year are all given.
Question 7: Requires only the last name of the President
Question 8: Requires only the last name of the previous President.
Question 9: Does not need to be verified. It is scored as correct if a female first name plus a last name other than the participant's last name is given.
Question 10: Requires that the entire series must be performed correctly in order to be scored as correct. Any error in the series or unwillingness to attempt the series is scored as incorrect.

Adjustment factor: Subtract 1 from Error Score if subject had only grade school education. Add 1 to error score if subject has had education beyond high school.

APPENDIX C: Beliefs About Medicines Questionnaire

Your Views about Medications Prescribed for You

- We would like to ask you about your personal views about medicines prescribed for you.
- These are statements other people have made about their medicines.
- Please indicate the extent to which you agree or disagree with them by ticking the appropriate box.
- There are no right or wrong answers. We are interested in your personal views.

	Strongly Agree	**Agree**	**Unsure**	**Disagree**	**Strongly Disagree**
My health, at present, depends on my medicines.					
Having to take medicines worries me.					
My life would be impossible without my medicines.					
Without my medicines I would be very ill.					
I sometimes worry about long-term effects of my medicines.					
My medicines are a mystery to me.					
My health in the future will depend on my medicines.					
My medicines disrupt my life.					
I sometimes worry about becoming too dependent on my medicines.					
My medicines protect me from becoming worse.					

APPENDIX D: Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Table 1. 2002 Criteria for Potentially Inappropriate Medication Use in Older Adults: Independent of Diagnoses or Conditions

Drug	Concern	Severity Rating (High or Low)
Propoxyphene (Darvon) and combination products (Darvon with ASA, Darvon-N, and Darvocet-N)	Offers few analgesic advantages over acetaminophen, yet has the adverse effects of other narcotic drugs.	Low
Indomethacin (Indocin and Indocin SR)	Of all available nonsteroidal anti-inflammatory drugs, this drug produces the most CNS adverse effects.	High
Pentazocine (Talwin)	Narcotic analgesic that causes more CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs. Additionally, it is a mixed agonist and antagonist.	High
Trimethobenzamide (Tigan)	One of the least effective antiemetic drugs, yet it can cause extrapyramidal adverse effects.	High
Muscle relaxants and antispasmodics: methocarbamol (Robaxin), carisoprodol (Soma), chlorzoxazone (Paraflex), metaxalone (Skelaxin), cyclobenzaprine (Flexeril), and oxybutynin (Ditropan). Do not consider the extended-release Ditropan XL.	Most muscle relaxants and antispasmodic drugs are poorly tolerated by elderly patients, since these cause anticholinergic adverse effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.	High
Flurazepam (Dalmane)	This benzodiazepine hypnotic has an extremely long half-life in elderly patients (often days), producing prolonged sedation and increasing the incidence of falls and fracture. Medium- or short-acting benzodiazepines are preferable.	High
Amitriptyline (Elavil), chlordiazepoxide-amitriptyline (Limbitrol), and perphenazine-amitriptyline (Triavil)	Because of its strong anticholinergic and sedation properties, amitriptyline is rarely the antidepressant of choice for elderly patients.	High
Doxepin (Sinequan)	Because of its strong anticholinergic and sedating properties, doxepin is rarely the antidepressant of choice for elderly patients.	High
Meprobamate (Miltown and Equanil)	This is a highly addictive and sedating anxiolytic. Those using meprobamate for prolonged periods may become addicted and may need to be withdrawn slowly.	High
Doses of short-acting benzodiazepines: doses greater than lorazepam (Ativan), 3 mg; oxazepam (Serax), 60 mg; alprazolam (Xanax), 2 mg; temazepam (Restoril), 15 mg; and triazolam (Halcion), 0.25 mg	Because of increased sensitivity to benzoadiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximums.	High
Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol) clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene)	These drugs have a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.	High
Disopyramide (Norpace and Norpace CR)	Of all antiarrhythmic drugs, this is the most potent negative inotrope and therefore may induce heart failure in elderly patients. It is also strongly anticholinergic. Other antiarrhythmic drugs should be used.	High
Digoxin (Lanoxin) (should not exceed >0.125 mg/d except when treating atrial arrhythmias)	Decreased renal clearance may lead to increased risk of toxic effects.	Low
Short-acting dipyridamole (Persantine). Do not consider the long-acting dipyridamole (which has better properties than the short-acting in older adults) except with patients with artificial heart valves	May cause orthostatic hypotension.	Low
Methyldopa (Aldomet) and methyldopa-hydrochlorothiazide (Aldoril)	May cause bradycardia and exacerbate depression in elderly patients.	High
Reserpine at doses >0.25 mg	May induce depression, impotence, sedation, and orthostatic hypotension.	Low
Chlorpropamide (Diabinese)	It has a prolonged half-life in elderly patients and could cause prolonged hypoglycemia. Additionally, it is the only oral hypoglycemic agent that causes SIADH.	High
Gastrointestinal antispasmodic drugs: dicyclomine (Bentyl), hyoscyamine (Levsin and Levsinex), propantheline (Pro-Banthine), belladonna alkaloids (Donnatal and others), and clidinium-chlordiazepoxide (Librax)	GI antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).	High
Anticholinergics and antihistamines: chlorpheniramine (Chlor-Trimeton), diphenhydramine (Benadryl), hydroxyzine (Vistaril and Atarax), cyproheptadine (Periactin), promethazine (Phenergan), tripelennamine, dexchlorpheniramine (Polaramine)	All nonprescription and many prescription antihistamines may have potent anticholinergic properties. Nonanticholinergic antihistamines are preferred in elderly patients when treating allergic reactions.	High
Diphenhydramine (Benadryl)	May cause confusion and sedation. Should not be used as a hypnotic, and when used to treat emergency allergic reactions, it should be used in the smallest possible dose.	High
Ergot mesyloids (Hydergine) and cyclandelate (Cyclospasmol)	Have not been shown to be effective in the doses studied.	Low
Ferrous sulfate >325 mg/d	Doses >325 mg/d do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.	Low
All barbiturates (except phenobarbital) except when used to control seizures	Are highly addictive and cause more adverse effects than most sedative or hypnotic drugs in elderly patients.	High

(continued)

Table 1. 2002 Criteria for Potentially Inappropriate Medication Use in Older Adults: Independent of Diagnoses or Conditions (cont)

Drug	Concern	Severity Rating (High or Low)
Meperidine (Demerol)	Not an effective oral analgesic in doses commonly used. May cause confusion and has many disadvantages to other narcotic drugs.	High
Ticlopidine (Ticlid)	Has been shown to be no better than aspirin in preventing clotting and may be considerably more toxic. Safer, more effective alternatives exist.	High
Ketorolac (Toradol)	Immediate and long-term use should be avoided in older persons, since a significant number have asymptomatic GI pathologic conditions.	High
Amphetamines and anorexic agents	These drugs have potential for causing dependence, hypertension, angina, and myocardial infarction.	High
Long-term use of full-dosage, longer half-life, non–COX-selective NSAIDs: naproxen (Naprosyn, Avaprox, and Aleve), oxaprozin (Daypro), and piroxicam (Feldene)	Have the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.	High
Daily fluoxetine (Prozac)	Long half-life of drug and risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation. Safer alternatives exist.	High
Long-term use of stimulant laxatives: bisacodyl (Dulcolax), cascara sagrada, and Neoloid except in the presence of opiate analgesic use	May exacerbate bowel dysfunction.	High
Amiodarone (Cordarone)	Associated with QT interval problems and risk of provoking torsades de pointes. Lack of efficacy in older adults.	High
Orphenadrine (Norflex)	Causes more sedation and anticholinergic adverse effects than safer alternatives.	High
Guanethidine (Ismelin)	May cause orthostatic hypotension. Safer alternatives exist.	High
Guanadrel (Hylorel)	May cause orthostatic hypotension.	High
Cyclandelate (Cyclospasmol)	Lack of efficacy.	Low
Isoxsurpine (Vasodilan)	Lack of efficacy.	Low
Nitrofurantoin (Macrodantin)	Potential for renal impairment. Safer alternatives available.	High
Doxazosin (Cardura)	Potential for hypotension, dry mouth, and urinary problems.	Low
Methyltestosterone (Android, Virilon, and Testrad)	Potential for prostatic hypertrophy and cardiac problems.	High
Thioridazine (Mellaril)	Greater potential for CNS and extrapyramidal adverse effects.	High
Mesoridazine (Serentil)	CNS and extrapyramidal adverse effects.	High
Short acting nifedipine (Procardia and Adalat)	Potential for hypotension and constipation.	High
Clonidine (Catapres)	Potential for orthostatic hypotension and CNS adverse effects.	Low
Mineral oil	Potential for aspiration and adverse effects. Safer alternatives available.	High
Cimetidine (Tagamet)	CNS adverse effects including confusion.	Low
Ethacrynic acid (Edecrin)	Potential for hypertension and fluid imbalances. Safer alternatives available.	Low
Desiccated thyroid	Concerns about cardiac effects. Safer alternatives available.	High
Amphetamines (excluding methylphenidate hydrochloride and anorexics)	CNS stimulant adverse effects.	High
Estrogens only (oral)	Evidence of the carcinogenic (breast and endometrial cancer) potential of these agents and lack of cardioprotective effect in older women.	Low

Abbreviations: CNS, central nervous system; COX, cyclooxygenase; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

Table 2. 2002 Criteria for Potentially Inappropriate Medication Use in Older Adults: Considering Diagnoses or Conditions

Disease or Condition	Drug	Concern	Severity Rating (High or Low)
Heart failure	Disopyramide (Norpace), and high sodium content drugs (sodium and sodium salts [alginate bicarbonate, biphosphate, citrate, phosphate, salicylate, and sulfate])	Negative inotropic effect. Potential to promote fluid retention and exacerbation of heart failure.	High
Hypertension	Phenylpropanolamine hydrochloride (removed from the market in 2001), pseudoephedrine; diet pills, and amphetamines	May produce elevation of blood pressure secondary to sympathomimetic activity.	High
Gastric or duodenal ulcers	NSAIDs and aspirin (>325 mg) (coxibs excluded)	May exacerbate existing ulcers or produce new/additional ulcers.	High
Seizures or epilepsy	Clozapine (Clozaril), chlorpromazine (Thorazine), thioridazine (Mellaril), and thiothixene (Navane)	May lower seizure thresholds.	High
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipyridamole (Persantin), ticlopidine (Ticlid), and clopidogrel (Plavix)	May prolong clotting time and elevate INR values or inhibit platelet aggregation, resulting in an increased potential for bleeding.	High
Bladder outflow obstruction	Anticholinergics and antihistamines, gastrointestinal antispasmodics, muscle relaxants, oxybutynin (Ditropan), flavoxate (Urispas), anticholinergics, antidepressants, decongestants, and tolterodine (Detrol)	May decrease urinary flow, leading to urinary retention.	High
Stress incontinence	α-Blockers (Doxazosin, Prazosin, and Terazosin), anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride), and long-acting benzodiazepines	May produce polyuria and worsening of incontinence.	High
Arrhythmias	Tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	Concern due to proarrhythmic effects and ability to produce QT interval changes.	High
Insomnia	Decongestants, theophylline (Theodur), methylphenidate (Ritalin), MAOIs, and amphetamines	Concern due to CNS stimulant effects.	High
Parkinson disease	Metoclopramide (Reglan), conventional antipsychotics, and tacrine (Cognex)	Concern due to their antidopaminergic/ cholinergic effects.	High
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, and muscle relaxants. CNS stimulants: dextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), and pemolin	Concern due to CNS-altering effects.	High
Depression	Long-term benzodiazepine use. Sympatholytic agents: methyldopa (Aldomet), reserpine, and guanethidine (Ismelin)	May produce or exacerbate depression.	High
Anorexia and malnutrition	CNS stimulants: DextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), pemolin, and fluoxetine (Prozac)	Concern due to appetite-suppressing effects.	High
Syncope or falls	Short- to intermediate-acting benzodiazepine and tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	May produce ataxia, impaired psychomotor function, syncope, and additional falls.	High
SIADH/hyponatremia	SSRIs: fluoxetine (Prozac), citalopram (Celexa), fluvoxamine (Luvox), paroxetine (Paxil), and sertraline (Zoloft)	May exacerbate or cause SIADH.	Low
Seizure disorder	Bupropion (Wellbutrin)	May lower seizure threshold.	High
Obesity	Olanzapine (Zyprexa)	May stimulate appetite and increase weight gain.	Low
COPD	Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol), clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene). β-blockers: propranolol	CNS adverse effects. May induce respiratory depression. May exacerbate or cause respiratory depression.	High
Chronic constipation	Calcium channel blockers, anticholinergics, and tricyclic antidepressant (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	May exacerbate constipation.	Low

Abbreviations: CNS, central nervous systems; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio; MAOIs, monoamine oxidase inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SSRIs, selective serotonin reuptake inhibitors.

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May 23, 2008

Todd Ruppar
University of Missouri
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APPENDIX E: MEMS Use Questions

MEMS Use Questions to be Asked One Week After Visit 1

1. Do you have any questions about using the MEMS or MEMS diary? Tell me about how you are using them.
2. Are you taking your medications directly from the electronic monitoring medication bottle for each dose? (e.g., not triggering the cap or routinely taking several doses out at once)
3. Have you written in the MEMS diary this week, for example, when you've refilled your MEMS bottle?
4. Are you having any problems with taking your medications related to using the MEMS?

APPENDIX F: Medication Information Card for Participants

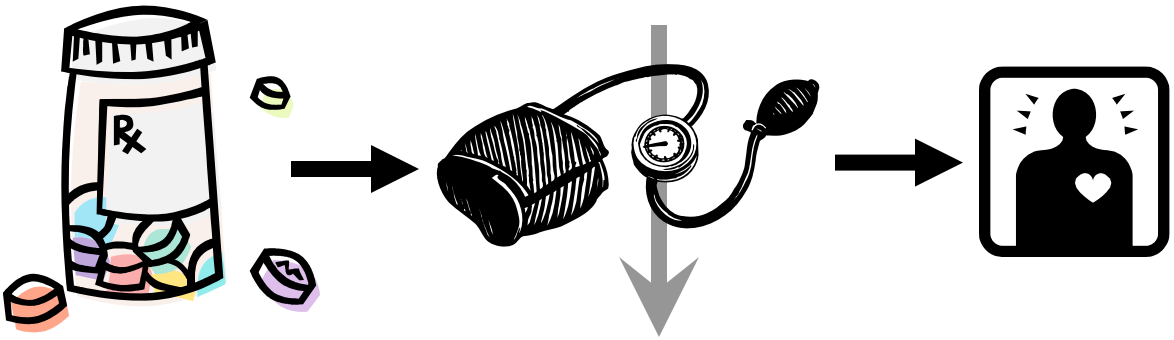
Information About Your Medicine

Name:	Date:

How to use this chart:

- This chart shows you when to take each of your medicines.
- At each of the times, look to see how much of each medication to take at that time.
- Medicines that you take only when needed are not included on this chart.

	Times to Take Medicine			
Medicine & Dosage				



APPENDIX G: Participant Diary Card

MEMS Cap Diary Card

- Please use this card to note any times you open your MEMS bottle for a reason other than taking your medicine.
- If you have any problems with your medication bottle, please call Todd Ruppar at _____.

Date	Time	Reason for Opening

Date	Time	Reason for Opening

APPENDIX H: Study Consent Form

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

INVESTIGATOR'S NAME: TODD RUPPAR, PHD(C), RN, GCNS-BC
PROJECT # 1114797
DATE OF PROJECT APPROVAL: JUNE 18, 2008

FOR HS IRB USE ONLY
APPROVED
HS IRB Authorized Representative — Date: 6/18/08
EXPIRATION DATE: 6-18-2009

STUDY TITLE: INTERVENTIONS TO IMPROVE MEDICATION-TAKING BEHAVIOR IN OLDER ADULTS WITH HYPERTENSION: AN EXPLORATORY STUDY

INTRODUCTION

This consent may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand.

This is a research study. Research studies include only people who choose to participate. As a study participant you have the right to know about the procedures that will be used in this research study so that you can make the decision whether or not to participate. The information presented here is simply an effort to make you better informed so that you may give or withhold your consent to participate in this research study.

Please take your time to make your decision and discuss it with your family and friends.

You are being asked to take part in this study because you have high blood pressure.

This study is being sponsored by the John A. Hartford Foundation and the American Academy of Nursing.

In order to participate in this study, it will be necessary to give your written consent.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test an intervention to help older adults do a better job of taking blood pressure medication as prescribed by their health care providers.

This research is being done because it is important to take blood pressure medicine every day as prescribed in order to prevent serious health problems from high blood pressure. Unfortunately, many people have a difficult time taking medications regularly.

How Many People Will Take Part In The Study?

About 100 people in the Columbia, Missouri and St. Louis, Missouri areas will take part in the screening process to identify 15 people who qualify to participate in this study.

What Is Involved in the Study?

Visit 1 – Screening
At the first study visit you will be asked to provide some information about yourself, and asked questions to make sure you qualify for the study. You will be asked some questions about your medical history, and will be asked about the medications you are taking. You will also be asked to participate in tests to check your memory and thinking ability, and given a short questionnaire to find out your thoughts about medications. Your blood pressure will be checked. Finally, we will place your blood pressure medication in a medication bottle with a special cap that will track when you take your medicine. If you take more than one blood pressure medication, we will do this with only one of your medicines. You will use this special medication bottle and cap throughout the rest of the study. You will be given a diary card on which to note any times you open your special medication bottle for any reason other than taking your medication, such as for refilling the bottle with new medicine. This visit is expected to take about 45 minutes. You will also receive a telephone call about one week after this visit to see how you are doing with using the special medication bottle caps.

Visit 2 – Week 0
Visit 2 will take place about 6 weeks after Visit 1, and may last between 30 minutes to about 60 minutes, depending on your study group placement. At this visit, we check your blood pressure and review your diary card for any accidental or extra medication cap openings. Your medication-taking information will be downloaded from the special medication cap to a computer. If your medication-taking is at or below a certain level, you will be asked to continue in the study.

At this point you will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor the researcher will choose what group you will be in. You will have an equal chance of being placed in any group.

Control Group:
After randomization, control group participants will continue to use special medication caps for their blood pressure medication and keep track of extra openings on their diary card. Control group participants will be seen again for the study at 12 weeks and 20 weeks after visit 2.

Intervention Group:
Half of the participants will be randomized into the intervention group. These participants will receive extra information about their blood pressure medications. We will talk to intervention group participants about their medication-taking habits and may suggest things to try to improve medication-taking. They will also be given a different type of electronic cap for their blood pressure medication bottle.

Intervention Visits – Weeks 2, 4, 6, & 8 after randomization
Participants **in the intervention group** will also have four brief extra visits. These will be scheduled at 2, 4, 6, and 8 weeks after Visit 2. At these visits we will check your blood pressure and download your medication-taking information from your medication bottle cap. Intervention group participants will be shown their blood pressure and also how well they have been taking their medications. These intervention visits are expected to take about 20 to 30 minutes each.

Visit 3 – Week 12 – Both Groups
At this visit, you will be seen and asked about any changes in their health and about any medication changes. Your blood pressure will be checked and medication-taking information will be downloaded from your special medication cap. Your diary card of extra or accidental cap openings will be reviewed with you. You will also be asked to complete a short questionnaire about your thoughts about your medications. This visit is expected to take about 30 minutes.

Visit 4 – Week 20 – Both Groups
At this final study visit, you will be seen and asked about any changes in their health, or to their medications. Your blood pressure will be checked and your medication cap downloaded and collected. Your blood pressure medication will be returned to its usual pill bottle you used before you started the study. Your diary card of extra or accidental cap openings will be reviewed with you and collected. You will also be asked some questions at this visit about your experience in the study. This visit is expected to take about 30 to 45 minutes.

How Long Will I Be in the Study?

We think you will be in the study for about six months.

The investigator and/or your doctor may decide to take you off this study if you are determined not to be eligible for randomization, if it is determined to be in your medical best interest, or if new information becomes available.

You can stop participating at any time. Your decision to withdraw from the study will not affect in any way your medical care and/or benefits. If you decide to withdraw from the study, you will be asked to return your medication tracking cap to the investigator. The investigator will provide a means for you to return the cap at no cost to you.

What Are the Risks of the Study?

It is possible that you may become tired during the study interviews.
You may feel uncomfortable about having your medication-taking monitored.

You may become upset if one of the study tests indicates a problem of which you were unaware, such as unusually high blood pressure, or a possible problem with your memory or thinking ability. If a problem is identified, we can assist you in notifying your doctor so that further evaluation and treatment, if needed, can be provided to you.

The medication caps that we will give you to use on the vials are not child-proof so you will need to take precautions to keep your medications out of the reach of children.

For the reasons stated above the investigator will observe you closely while giving the study intervention described and, if you have any worrisome symptoms or symptoms that the investigator or his associates have described to you, notify the investigator immediately. Todd Ruppar's telephone number is 314-591-5259. For more information about risks and side effects, ask the investigator or contact Todd Ruppar at 314-591-5259.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. You may expect to benefit from taking part in this research to the extent that you are contributing to medical knowledge. We hope the information learned from this study will benefit other patients with high blood pressure in the future.

Other benefits include free blood pressure checks and home visits from a nurse who will review your medicines with you.

There is no guarantee that taking part in this research will result in any improvement in your condition.

WHAT OTHER OPTIONS ARE THERE?

An alternative is to not participate in this research study.

If you have questions or concerns about study participation, you may discuss them and your options with the study investigator and your doctor.

WHAT ABOUT CONFIDENTIALITY?

Information produced by this study will be stored in the investigator's file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate, secure location. Information contained in your records may not be given to anyone unaffiliated with the study in a form that could identify you without your written consent, except as required by law. If the investigator conducting this study is not your primary, or regular doctor, he must obtain your permission before contacting your regular doctor for information about your past medical history or to inform them that you are in this trial.

It is possible that your medical and/or research record, including sensitive information and/or identifying information, may be inspected and/or copied by the study sponsor (and/or its agent), the Food and Drug Administration (FDA), federal or state government agencies, or hospital accrediting agencies, in the course of carrying out their duties. If your record is inspected or copied by the study sponsor (and/or its agents), or by any of these agencies, the University of Missouri will use reasonable efforts to protect your privacy and the confidentiality of your medical information.

The results of this study may be published in a medical book or journal or used for teaching purposes. However, your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

WHAT ARE THE COSTS?

Taking part in this study will not lead to added costs to you or your insurance company.

WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

You will be compensated a total of $50 for completion of the duration of the study. You will be paid $25 after Visit 3 and the remaining $25 after completion of the study.

WHAT IF I AM INJURED?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury. The University of Missouri, in fulfilling its public responsibility, has provided medical, professional and general liability insurance coverage for any injury in the event such injury is caused by the negligence of the University of Missouri, its faculty and staff. The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while participating in the research projects of the University of Missouri. In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number (573) 882-1181, at the Health Sciences Center, who can review the matter and provide further information. This statement is not to be construed as an admission of liability.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Participation in this study is voluntary. You do not have to participate in this study. Your present or future care will not be affected should you choose not to participate. If you decide to participate, you can change your mind and drop out of the study at any time without affecting your present or future care. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. In addition, the investigator of this study may decide to end your participation in this study at any time after he has explained the reasons for doing so and has helped arrange for your continued care by your own doctor, if needed.

You will be informed of any significant new findings discovered during the course of this study that might influence your health, welfare, or willingness to continue participation in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions regarding your rights as a participant in this research and/or concerns about the study, or if you feel under any pressure to enroll or to continue to participate in this study, you may contact the University of Missouri Health Sciences Institutional Review Board (which is a group of people who review the research studies to protect participants' rights) at (573) 882-3181.

You may ask more questions about the study at any time. For questions about the study or a research-related injury, contact Todd Ruppar, RN at 314-591-5259.

A copy of this consent form will be given to you to keep.

SIGNATURE

I confirm that the purpose of the research, the study procedures, the possible risks and discomforts as well as potential benefits that I may experience have been explained to me. Alternatives to my participation in the study also have been discussed. I have read this consent form and my questions have been answered. My signature below indicates my willingness to participate in this study.

Subject/Patient*	Date
Legal Guardian/Advocate/Witness (if required)**	Date
Additional Signature (if required) (identify relationship to subject)***	Date

*A minor's signature on this line indicates his/her assent to participate in this study. A minor's signature is not required if he/she is under 7 years old. Use the "Legal Guardian/Advocate/Witness" line for the parent's signature, and you may use the "Additional Signature" line for the second parent's signature, if required.

**The presence and signature of an impartial witness is required during the entire informed consent discussion if the patient or patient's legally authorized representative is unable to read.

***The "Additional Signature" line may be used for the second parent's signature, if required. This line may also be used for any other signature which is required as per federal, state, local, sponsor and/or any other entity requirements.

"If required" means that the signature line is signed only if it is required as per federal, state, local, sponsor and/or any other entity requirements.

SIGNATURE OF STUDY REPRESENTATIVE

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered questions regarding the study to the best of my ability.

Study Representative****	Date

****Study Representative is a person authorized to obtain consent. Per the policies of the University of Missouri Health Care, for any 'significant risk/treatment' study, the Study Representative must be a physician who is either the Principal or Co-Investigator. If the study is deemed either 'significant risk/non-treatment' or 'minimal risk,' the Study Representative may be a non-physician study investigator.

APPENDIX I: Study Source Documents

Medication Adherence in Hypertension Study

University of Missouri—Columbia Sinclair School of Nursing

Visit 1 (Screening) Date: _____ Participant Number: _____

Visit Start Time: _____ Visit End Time: _____

□ Informed consent obtained prior to any study procedures

DOB: _____ Gender: □ Male □ Female

Level of Education: □ Grade School □ Some high school education
□ Completed High school □ Beyond high school education

Medical History:

□ Hypertension Approximate year of diagnosis (or # of years): _____

Diagnosis	Approx. year of diagnosis (or # of years with dx)

□ Medication regimen recorded

□ SPMSQ Administered

□ BMQ Completed by participant

Blood Pressure: _____ Arm: □ Left □ Right (only if L arm contraindicated)

MEMS cap number: _____ Medication info (name/freq): _____
_____

□ Participant instructed on the use of MEMS cap.

□ Participant given MEMS diary with instructions for use.

□ Scheduled Visit 2 (min. 6 weeks) Date: _____ Time: _____

Comments: _____
_____
_____
_____

Medication Adherence in Hypertension Study

University of Missouri—Columbia Sinclair School of Nursing

Visit 1 (Screening) Date: _____ Participant Number: _____

Inclusion/Exclusion Criteria

Inclusion Criteria:	Criteria Met	Criteria Not Met
1) Participants will be aged 60 years or greater at time of study entry.		
2) Participants must be able to read, write, and converse in English.		
3) Participants will have a diagnosis of hypertension (based on participant report).		
4) Participants will have an active prescription for at least one antihypertensive medication with no antihypertensive prescription changes for 30 days at the time of study entry.		
5) Participants must self-administer his or her own medications without prompts from any other person or device.		
6) Baseline medication adherence rate of < 85%.		
7) Participants must be free of cognitive deficit as determined by a score of "normal" (adjusted score of 0 – 2) on the Short Portable Mental Status Questionnaire (SPMSQ).		
8) Participants agree to complete all study contacts and measurements, including the use a special medication bottle with a Medication Event Monitoring System (MEMS) cap for the duration of the study.		
9) Able to open and close MEMS caps.		
Exclusion Criteria:		
1) Participant is in state of severe hypertension (BP of >180/120 mmHg) at the time of study enrollment. Participants presenting with severely elevated blood pressure will be referred to their primary care provider.		
2) Participant resides in a residential facility where medications are administered by facility staff. Participants who reside in assisted living facilities but maintain control of their medications remain eligible.		
3) Participant has a terminal chronic illness with a life expectancy of six months or less.		

Medication Adherence in Hypertension Study

University of Missouri—Columbia Sinclair School of Nursing

Visit 1 (Screening) Date: _____ Participant Number: _____

Number of Rx medications: _____ Number of OTC medications: _____

Medication Name	Dose	Freq.	Indication	Approx. number of years or mo. taken

Medication Adherence in Hypertension Study

University of Missouri—Columbia Sinclair School of Nursing

Phone Contact (Week -5) Date: _____ Participant Number: _____

MEMS Use Questions to be Asked One Week After Visit 1

1. Do you have any questions about using the MEMS or MEMS diary? Tell me about how you are using them.

Comments: _____
_____
_____

2. Are you taking your medications directly from the electronic monitoring medication bottle for each dose? (e.g., not triggering the cap or routinely taking several doses out at once)

Comments: _____
_____
_____

3. Have you written in the MEMS diary this week, for example, when you've refilled your MEMS bottle?

Comments: _____
_____
_____

4. Are you having any problems with taking your medications related to using the MEMS?

Comments: _____
_____
_____

Medication Adherence in Hypertension Study

University of Missouri—Columbia Sinclair School of Nursing

Visit 2 (Week 0) Date: _____ Participant Number: _____

Visit Start Time: _____ Visit End Time: _____

□ Confirmed continued consent to participate in study

□ MEMS cap downloaded and adjustments from diary made as needed

Adherence rate over past 2 weeks: _____

If adherence <85%, participant may be enrolled.

□ Measured blood pressure: _____

Treatment Assignment: □ Tx group □ Control group

□ Recorded any changes to medications

MEMS cap number: _____

□ Participant instructed on the use of MEMS cap.

□ Participant given MEMS diary with instructions for use.

□ Scheduled Visit 3 (approx. 12 weeks) Date: _____ Time: _____

Comments: _____

_____

_____

Tx Group Only:

□ Complete medication card with participant and help participant decide where to keep card

Location: _____

□ Review medication regimen with participant and provide hypertension education.

□ Conduct habit analysis

□ Conduct medication skills assessment:

	Yes	No
Able to open medication bottle	□	□
Able to read medication instructions	□	□
Has sufficient dexterity to handle pills and accurately self-administer meds	□	□

□ Interventions/assistive devices provided for any skills marked "No"

□ BP and adherence feedback provided to participant, and BP recorded on diary

□ Scheduled Visits 2A through 2D

Visit 2A (Week2) Date: _____ Participant Number: _____

Visit Start Time: _____ Visit End Time: _____

□ Confirmed continued consent to participate in study

□ Recorded any changes to medications and updated participant's medication card

□ Ask about integration of medication-taking habits into daily routines

□ Downloaded MEMS cap data □ Measured blood pressure: _____

Percent adherent: _____

□ Feedback provided to participant and BP recorded on diary

□ Confirmed next appointment date & time

Comments: _____

_____

_____

_____

Visit 2B (Week 4) Date: _____

Visit Start Time: _____ Visit End Time: _____

□ Confirmed continued consent to participate in study

□ Recorded any changes to medications and updated participant's medication card

□ Ask about integration of medication-taking habits into daily routines

□ Downloaded MEMS cap data □ Measured blood pressure: _____

Percent adherent: _____

□ Feedback provided to participant and BP recorded on diary

□ Confirmed next appointment date & time

Comments: _____

_____

_____

_____

Visit 2C (Week 6) Date: _____ Participant Number: _____

Visit Start Time: _____ Visit End Time: _____

□ Confirmed continued consent to participate in study

□ Recorded any changes to medications and updated participant's medication card

□ Ask about integration of medication-taking habits into daily routines

□ Downloaded MEMS cap data □ Measured blood pressure: _____

Percent adherent: _____

□ Feedback provided to participant and BP recorded on diary

□ Confirmed next appointment date & time

Comments: _____

_____

_____

_____

Visit 2D (Week 8) Date: _____

Visit Start Time: _____ Visit End Time: _____

□ Confirmed continued consent to participate in study

□ Recorded any changes to medications and updated participant's medication card

□ Ask about integration of medication-taking habits into daily routines

□ Downloaded MEMS cap data □ Measured blood pressure: _____

Percent adherent: _____

□ Feedback provided to participant and BP recorded on diary

□ Changed MEMS cap from SmartCap back to TrackCap

MEMS Cap number: _____

□ Confirmed next appointment date & time

Comments: _____

_____

_____

_____

Medication Adherence in Hypertension Study

University of Missouri—Columbia Sinclair School of Nursing

Visit 3 (Week 12) Date: _____ Participant Number: _____

Visit Start Time: _____ Visit End Time: _____

□ Confirmed continued consent to participate in study

□ Recorded any changes to medical history

□ Recorded any changes to medications

□ BMQ completed by participant

□ Collect and review MEMS diary card

□ Downloaded MEMS cap data □ Measured blood pressure: _____

Percent adherent: _____

Comments: _____

_____

_____

_____

VITA

Todd M. Ruppar received his Bachelor of Science in Nursing and Master of Science in Gerontological Nursing degrees from Saint Louis University in St. Louis, Missouri. He has worked in several clinical nursing areas in acute care, community health, and long-term care, and is a board-certified gerontological clinical nurse specialist. He has extensive experience coordinating clinical trials and conducting longitudinal studies of aging and cognition. In 2005, Mr. Ruppar entered the doctoral program at the University of Missouri Sinclair School of Nursing, and in 2007 became a John A. Hartford Foundation Building Academic Geriatric Nursing Capacity Scholar.