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# Evidence-based Recommendations for Increasing Pharmacologic Knowledge of Hypertensive Adult Patients with Low Pharmacologic Literacy

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EVIDENCE-BASED RECOMMENDATIONS FOR INCREASING  
PHARMACOLOGIC KNOWLEDGE OF HYPERTENSIVE ADULT PATIENTS  
WITH LOW PHARMACOLOGIC LITERACY

A project submitted in partial fulfillment  
of the requirements for the degree of  
Master of Science in Nursing

By

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## **Abstract**

Medication nonadherence associated with inadequate knowledge of medications has been an enduring clinical problem among hypertensive adult patients. The combination of inadequate health literacy and medication nonadherence of hypertensive adult patients has been a major cause of uncontrolled hypertension. Several studies suggested inadequate or incorrect knowledge of medications in hypertensive adult patients was correlated with non-adherence to their antihypertensive medications. The challenge of inadequate pharmacologic knowledge among hypertensive adult patients must be overcome for two reasons. First, prescription medications play an extremely important role in managing hypertension. Second, hypertension is a significant healthcare concern in North America.

The purpose of this project was to develop evidence-based recommendations for increasing pharmacologic knowledge for hypertensive adult patients with low pharmacologic literacy. The recommendations were formulated based on careful research and appraisal of most current evidences pertinent to the topic. The model used for this project was the Iowa Model of Evidence-Based Practice to Promote Quality Care.

Evidences strongly suggested educational content regarding antihypertensive medications must be limited in scope and presented simply. Educational material design should be simple and straightforward. Evidences also pointed to the importance of instructing patients to monitor and record daily blood pressure at home.

Key words: education, medication adherence, medication knowledge, antihypertensive medications, health literacy, teaching methods, instruction designs and materials

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## **Chapter 1: Introduction**

### **Significance of the Problem**

Medication nonadherence has perpetually been a major issue among hypertensive adult patients. Two important factors associated with increased nonadherence are higher copayments for antihypertensive medications (AHM's) (World Health Organization, 2003; Chobanian, 2009; Pittman et al., 2010) and inadequate knowledge of AHM's (Pittman et al., 2010; Hacıhasanoğlu & Gözümlü, 2011; Abdeesco, 2012). For example, a copayment of \$10 or more was likely to discourage patients from adhering to their prescription (World Health Organization, 2003; Chobanian, 2009; Pittman et al., 2010).

Several studies have suggested inadequate knowledge of medications correlate with limited health literacy and negative health outcomes such as poor medication refill (Gazmararian, Williams, Peel, & Baker, 2003; Torres & Marks, 2009; Persell, Osborn, Richard, Skripkauskas, & Wolf, 2007). Osborn, Paasche-Orlow, Bailey, & Wolf (2011) found patient knowledge played an important role in linking health literacy to health outcomes for patients with hypertension. Gazmararian, Kripalani, Miller, Echt, Junling, and Rask (2006) compared patient health literacy, levels of education, socioeconomic and ethnic backgrounds, and medication complexities. They found patients with inadequate health literacy to have lower likelihood of refilling their medications.

The concept of health literacy was introduced in 1974 (Simonds, 1974). Since then, health literacy has become increasingly important. Sørensen et al. (2012) defined health literacy as “people’s knowledge, motivation and competences to access, understand, appraise, and apply health information in order to make judgments and take decisions in everyday life concerning healthcare, disease prevention and health

promotion to maintain or improve quality of life during the life course” (p. 3). Health literacy of patients have been determined by Test of Functional Health in Adults or TOFHLA, an instrument for measuring how much a patient can understand and use basic health information (Weiss et al., 2005). Patients have been tested on medical information and instructions about various scenarios. The score ranged between 0 to 100 points (Committee on Health Literacy, 2004). Since 1974, many health literacy instruments have been developed and variously adapted to overcome demographic, linguistic, and cultural barriers, such as Rapid Estimate of Adult Literacy in Medicine (Davis, Crouch, & Long, 1993) and Newest Vital Sign (Weiss et al., 2005).

The challenge of inadequate health literacy among hypertensive adult patients must be addressed for two reasons. First, prescription medications play an extremely important role in managing hypertension (Pittman et al, 2010). Since a relation has been established between low health literacy and poor medication adherence, healthcare providers need to educate patients in a manner that enables them to adhere to their medication regimens (Gazmararian et al., 2006). Second, hypertension is a significant healthcare concern in North America. The National Center for Health Statistics reported “the overall age-adjusted prevalence of hypertension among U.S. adults aged 18 and over was 28.6% in 2009–2010” (Yoon, Burt, Louis, & Carroll, 2012, p. 1). Hypertension was most prevalent among those aged 60 and older (67%) and non-Hispanic black persons (40%) (Yoon et al., 2012). While 81.9% of adults were aware of their hypertension, only 76.4% were currently taking medication to lower their blood pressure (BP) (U.S. Department of Health and Human Services, 2012).

The problem of medication nonadherence had detrimental consequences to

individual hypertensive adult patients. The consequences included target organ damage such as heart failure, stroke, chronic kidney disease, and retinopathy (The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 2003). This problem had negative implications for healthcare costs in the United States. In 2006, healthcare costs associated with complications related to medication nonadherence were estimated to be \$76.6 billion per year (Lloyd-Jones, 2010). Similarly, Pittman et al. (2010) conducted a 2-year retrospective study of the national pharmacy benefits database and medical claims among patients diagnosed with hypertension. They concluded adherence to AHM's significantly lowered total healthcare costs—a major factor being a substantial decrease in the rate of cardiovascular related emergency room visits and hospitalizations. One feasible solution to the increased healthcare costs and the detriments for patient wellbeing is to overcome the barriers of medication adherence.

### **Purpose of the Project**

The purpose of this project is to help patients understand their AHM's in order to increase medication adherence. More specifically, the project aims to increase knowledge of AHM's among hypertensive adult patients with inadequate pharmacologic literacy.

Educating patients is an integral component in the role of healthcare providers at the forefront of patient care, interfacing with patients in a variety of clinical settings. A challenge, however, for such healthcare providers is the constraints of limited time with patients. Communication takes time; education takes even more time. So, how do healthcare providers effectively and efficiently communicate and educate their patients within a limited amount of time they have with patients? One solution may be to apply

concepts from the field of study to create effective and efficient educational materials and communication methods appropriate for various patients.

## Chapter 2: Concept Analysis

### Concept Variables

Variables included in this project are antihypertensive medications (AHM's), health literacy, hypertension, hypertensive adult patients, and medication adherence.

According to *JNC 7* (The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 2003), there were five classes of antihypertensive medications: diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, and calcium channel blockers. These agents effectively lowered BP and, consequently, reduced or slowed progression of target organ damage such as left ventricular hypertrophy, myocardial infarction, heart failure, stroke, chronic kidney disease, peripheral arterial disease, and retinopathy (The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 2003).

Health literacy can be variously defined. However, the working definition adopted for this project is from Sørensen et al. (2012): “knowledge, motivation and competences to access, understand, appraise, and apply health information in order to make judgments and make decisions in everyday life concerning healthcare, disease prevention and health promotion to maintain or improve quality of life during the life course” (p. 3).

Hypertension is defined as systolic blood pressure (SBP)  $\geq$  140 mmHg and/or diastolic blood pressure (DBP)  $\geq$  90 mmHg (U.S. Department of Health and Human Services, 2003). Hypertensive adult patients have SBP  $\geq$  140 mmHg and/or DBP  $\geq$  90 mmHg with or without comorbidities such as diabetes and dyslipidemia.

Medication adherence refers to a patient's efforts to follow pharmacologic treatment recommendations mutually agreed upon by patient and healthcare provider (Resnik, 2005). It may be directly measured by BP and indirectly measured by pill counts, BP diaries, pharmacy refill records, and self-reported outcomes (Bartels, 2004; Vermeire, Hearnshaw, Van Royen, & Denekens, 2001).

### **Health Literacy**

Teaching and learning of pharmacologic interventions are directly related to the concept of health literacy. Effective communication and interactions between healthcare providers and patients are rooted in health literacy. Health literacy encompasses the ability to understand verbal and written information to function in a health-related context to achieve one's health-related goals (National Association of Adult Literacy, n.d.).

### **Antecedents of Health Literacy**

Antecedents of health literacy discussed in this paper are cognitive abilities and motivation (Levin-Zamir & Peterburg, 2001; Mancuso, 2008). Cognitive abilities involve oral and written literacy (Committee on Health Literacy, 2004). Health literacy goes beyond the basic skills and comprehension to include critical thinking skills—the ability to appraise and apply health information (Sørensen et al., 2012). In addition, healthcare providers are to motivate patients to “improve personal capacity to exert control over factors that determine health and improve health outcomes” (Levin-Zamir & Peterburg, 2001, p. 88). Patients must be motivated to cope with health issues and to improve health outcomes in terms of reduction in “mortality, morbidity, disability, dysfunction, quality of life, and functional dependence” (Nutbeam, 2000, p. 261). Motivation is an educational process in which healthcare providers help patients develop

a degree of self-awareness, knowledge, and skills, so patients may be able to assume responsibility for their health-related decisions (Feste & Anderson, 1995).

### **Attributes of Health Literacy**

Defining attributes of health literacy include cognitive ability, analytical ability, and social ability.

**Cognitive ability.** Health literacy requires innate potential and learned skills of the individual obtained through formal and informal education (Committee on Health Literacy, 2004). Cognitive ability is associated with emotional readiness to learn as well. Cognitive ability is a complex interplay between fundamental skills and an “ability to identify, understand, interpret, create, communicate, compute and use printed and written materials associated with varying contexts” (Richmond, Clinton, & Sachs-Israel, 2008, p. 18). Education to improve cognitive ability depends on effective communication between patients and healthcare providers. According to U.S. Health and Human Services (2003), effective health communication could take various forms through direct exchange and indirect exchanges between patients and providers through media such as audiovisual aids and the Internet. When patients understand a given set of instructions or descriptions of medications, they should be able to verbalize their understanding of the instructions and procedures in their own words.

**Analytical ability.** Analytical ability is concerned with an individual’s ability to think critically through significant oral and written materials. It is related to awareness in so far as it is directly related to a patient’s “ability to recognize that accurate and complete information is the basis for intelligent decision-making” (Frisch, Camerini, Diviani, & Schulz, 2012, p. 122). Critical thinking skills enable the individual to identify

and evaluate health information from different types of resources and media. Nutbeam (2000) explicitly referred to analytical ability as critical literacy—more advanced cognitive skills to critically analyze health-related data and to use it to make educated decisions in life events. Freedman, Bess, Tucker, Boyd, Tuchman, & Wallston (2009) proposed “An emphasis on evaluation underscored the importance of being able to judge or determine the significance, worth, or quality of information related to the health of the public” (p. 448). Patients with adequate analytical ability confidently asks relevant questions and requests clarification. They are better able to successfully navigate and negotiate the health delivery systems (Committee on Health Literacy, 2004). In addition, they recognize the importance of self-management and empowerment. Thus, they put into practice pertinent knowledge of healthcare, health promotion, and disease prevention.

**Social ability.** Social ability entails cultural and spiritual literacy. Zarcadoolas, Pleasant, and Greer (2003) referred to cultural literacy as “recognizing and using collective beliefs, customs, world-views, and social identity relationships to interpret and act on [as well as produce] health information” (p. 120). An individual with social ability is capable of “understanding, thinking, and responding to human experiences and world events” (Committee on Health Literacy, 2004, p. 34). As a result, such an individual is able to “actively participate in everyday activities, to extract information and derive meaning from different forms of communication, and to apply new information to changing circumstances” (Nutbeam, 2000, p. 264). In order to participate fully in a health-literate society, a patient must be able to interpret the meaning of social practices, which are influenced by “language, socioeconomic status, gender, race, and ethnicity,

along with influences of mass media as represented by news publishing, advertising, marketing, and the plethora of health information sources available through electronic sources” (Committee on Health Literacy, 2004, p. 34). Making informed decision should be congruent with one’s social, cultural, and spiritual background.

### **Case Model**

EJ was a 45-year-old African American male with a bachelor’s degree in computer engineering. He was diagnosed with hypertension 6 months ago during annual exam with a family nurse practitioner (FNP). The FNP effectively educated him in the disease process and treatment plans of hypertension. Individualized educational leaflets were well-organized, easy to read, and included pertinent information such as disease process, lifestyle modifications, medication names, dosages, use, and adverse effects. Within the leaflets, EJ could take notes and record his daily BP in the provided table. At the end of the visit, the FNP verified EJ’s understanding by asking him questions regarding what was taught. She was pleased he was able to verbalize what was taught in his own words. He was motivated to keep his BP below 140/90 mmHg, knowing uncontrolled hypertension could lead to stroke, retinopathy, as well as cardiovascular and renal complications. He complied with recommended lifestyle modification, took hydrochlorothiazide and lisinopril as prescribed, recorded his daily BP, weighed himself daily, and monitored for side effects of the medications such as cough. He also monitored for worsening symptoms of hypertension such as edema, dyspnea, and chest pain. He valued his health and believed in partnership with his FNP. During his 3-month follow up visit, the FNP was encouraged by EJ’s positive health outcome. She was also encouraged by his ability to communicate his progress in weight loss, BP control, feeling

of well-being, and satisfaction with the care the FNP provided. He asked pertinent questions and reviewed the use, side effects, and dosage administration.

EJ exemplified all three attributes of health literacy—cognitive, analytical, and social abilities. He had functional reading and comprehension skills, as evidenced by his ability to follow instructions and adhering to medication regimen. He synthesized the information and made educated decisions to change his behavior. Finally, he functioned successfully as a healthcare consumer by adopting healthful practices.

### **Interactions of Key Players of Concept**

The FNP and the patient were the key players. The FNP was aware of the importance of effectively educating the patient about his medications and ensuring understanding. She provided material as a source of reference and documented the patient's progress of BP control. On the other hand, the patient EJ exemplified all three attributes of health literacy—cognitive, analytical, and social abilities. He functioned as a healthcare consumer by adhering to AHM's and achieving positive health outcomes.

### **Application to the Project**

Evidence-based recommendations for increasing pharmacologic knowledge can be useful to healthcare providers when healthcare providers provide face-to-face pharmacologic education to hypertensive adult patients at discharge from a hospital, primary care setting, and skilled nursing facility. Education facilitates patients' understanding of the medications, medication adherence, and monitoring and controlling BP while at home. Implementing and evaluating the recommendations is beyond the scope of this project.

### **Chapter 3: Method and Framework**

The model used for this project is the Iowa Model of Evidence-Based Practice to Promote Quality Care. The model serves as a guide for healthcare providers in translating current research evidence into clinical practice for improvement of patient care. According to Titler et al. (2001), research evidence consists of findings from meta-analyses, RCTs, observational studies, and qualitative research. The Iowa Model of Evidence-Based Practice to Promote Quality Care contains seven steps: 1) select a topic, 2) form a team, 3) retrieve evidences, 4) grade evidences, 5) develop an evidence-based standard, 6) implement the evidence-based standard, and 7) evaluate the implementation of the evidence-based standard (Doody & Doody, 2011; Titler et al., 2001).

The first step of selecting a topic may occur through an organic process. However, it normally occurs when healthcare providers think critically on ways to improve the practice of patient care. Among many challenges and problems healthcare providers regularly face, health care providers may choose the topic with the highest priority. It may help to identify a topic that is most relevant to the needs of the organization to which healthcare providers belong (Titler et al., 2001). Furthermore, when deciding on a topic, healthcare providers must consider other factors such as “the magnitude of the problem, its application to all areas of practice, its contribution to improving care, the availability of data and evidence in the problem area, the multidisciplinary nature of the problem, and the commitment of staff” (Doody & Doody, 2011, p. 661).

As noted earlier, health literacy has a major impact and burden not only on individual patients, but also on the entire U.S. healthcare system. Likewise, hypertension

is a prevalent disease and the leading cause of cardiovascular complications (Yoon, Burt, Louis, & Carroll, 2012). Since patient's awareness and knowledge of medication encourages adherence to prescribed treatment, we may consider educating hypertensive adult patients as a high priority in providing healthcare in the U.S (Persell, Osborn, Richard, Skripkauskas, & Wolf, 2007). Furthermore, medication adherence eventually decreases morbidity and mortality from cardiovascular complications (The Joint National Committee, 2003). Independent of the broader implications of pharmacologic literacy among hypertensive adult patients, the lives and well-being of our patients are related to pharmacologic literacy.

Step two of the Iowa Model recommends a team assemble to study the selected topic. Team members may consist of a leader, stakeholders, healthcare providers, physicians, pharmacists, and specialists. Researchers are guided by the chosen topic and are responsible for developing a protocol based on research findings in the literature. The leader assigns a specific task for each team member. The team is responsible for implementing the standard and evaluating the process of changing a specific area of practice (Doody & Doody, 2011). Solely this author completed the project.

In accordance with step three of the Iowa model, related evidences were retrieved for this project. Retrieval process took three paths. First, systematic searches were performed in electronic databases such as Academic Search Complete, Alt HealthWatch, MED – The Allied and Complementary Medicine Database, CINAHL Plus with Full Text, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Education Research Complete, Health Source: Nursing/Academic Edition, MEDLINE, and MEDLINE with Full Text. Peer reviewed articles, RCT's, meta-

analysis, and meta-synthesis publications between 2003 and 2013 were specified in the searches. Key words used in the searches included hypertension, education, medication adherence, medication knowledge, patients and education, teaching and learning, antihypertensive medications, health literacy, teaching methods, instruction designs and materials, leaflets, and booklets. Second, evidence retrieval followed identified references within pertinent sources. This often resulted in locating primary sources. Third, standard guidelines accepted nationally were consulted. For example, the project incorporated guidelines from the National Institute of Health's Joint National Committee, Center for Healthcare Strategies, and Center for Disease Control.

Inclusion criteria were adult patients aged 18 years or older with intact mental status. The adult patients had primary or secondary hypertension with such comorbidities as heart failure, diabetes mellitus, or dyslipidemia. They could be on one or more AHM's. There were no limitations of geographical locations. Exclusion criteria were patients who were illiterate or had neurological deficits such as dementia. Patients with chronic kidney disease and dependence on dialysis were excluded.

While researching *hypertension education*, the author of this project came across 2,495 articles. As the searches were narrowed down to *blood pressure*, the number of articles decreased to 617 articles. The number of articles was further reduced to 293, when *antihypertensive medications* was specified. The number of articles decreased to 261 when *patient compliance* was specified. Out of 261 articles, only articles pertinent to content of AHM education and design were selected. The author managed the articles by dividing them into 3 categories: barriers to medication adherence, educational content, and format and style of educational material

According to the Iowa Model, subsequent to evidence retrieval, researchers are ready for step four in which evidences and guidelines are systematically evaluated. In order to appraise evidences and guidelines, researchers must understand the extent of the topic, pertinent concepts and theories, current state of practices, nature of qualitative and quantitative research methodologies, process of critiquing research, and the type and strength of evidence (Titler et al., 2001). The most current research evidences should be graded and categorized into four levels of evidence. Level 1 includes meta-analysis and one or more large RCT's. Level 2 includes one or more smaller RCT's or quasi-experimental studies. Level 3 includes cohort, case controlled, and observational studies. Level 4 includes expert opinion or consensus (The Joanna Briggs Institute, 2008). From the selected 27 articles, ten articles were classified as level 1, nine as level 2, four as level 3, and four as level 4.

In step five of the Iowa Model, researchers synthesize evidences into practice recommendations. In making recommendations of practice, healthcare providers should base decisions on feasibility, appropriateness, meaningfulness, and effectiveness. In this project, graded evidences were categorized into three recommendations. Grade A recommendation: strong support merits application in the area of feasibility, appropriateness, meaningfulness, and effectiveness. Grade B recommendation: moderate support warrants consideration of application in the four areas. Grade C recommendation: not supported (The Joanna Briggs Institute, 2008).

In step six, healthcare providers implement evidence-based practice. In order to do so, healthcare providers must take into consideration organization's written policy, procedures, and evidence-based guidelines. At the same time, healthcare providers must

ensure communication among direct-care providers, administrative staff, and leaders. Communication can be achieved through in-service education, audit, and feedback (Jamtvedt, Young, Kristoffersen, Thomson O Brien, & Oxman, 2004; Titler, 2004).

In the seventh and final step, healthcare providers evaluate implementation of the EBP. Titler et al. (2001) suggested, "Evaluation provides important information for other care providers, administrators, and policy makers" (p. 507). As part of a feedback loop, healthcare providers should disseminate evaluation data and insights from outcomes through presentations and publications (Titler et al., 2001). Steps six and seven are beyond the scope of this project.

### **Time Line of Project**

Literature review began in August 2013. This project did not require ethical approval from the Institutional Review Board because (IRB) the project did not involve direct interaction with patients. There was no potential harm to patients.

The project was presented to registered nurses and charge nurses at The Laurels of Massillon Skilled Nursing and Rehabilitation Center on October 23, 2013. The project was presented at Cedarville University to interested parties on November 21, 2013. The project was completed in December 2013.

Dr. Angelia Mickle is the chair of the project review committee. Another committee member is Dr. Aleda Chen.

## Chapter 4: Results

The recommendations to follow were formulated based on careful research of resources pertinent to the topic. Resources were organized into three groups: 1) barriers to medication adherence, 2) educational content, and 3) format and style of educational material. Literature review began after retrieval of evidences. Evidences from articles were appraised and graded, using the Iowa Model’s four levels of evidences. Based on the levels of evidences, recommendations were formulated, using the Iowa Model’s three grades (A, B, C) of recommendations (The Joanna Briggs Institute, 2008).

### Graded Review of Selected Literature

Table 1

#### *Barriers to Medication Adherence*

Authors	Title	Research Design	Results	Level of Evidence
Gazmararian, Kripalani, Miller, Echt, Junling, & Rask 2006	Factors Associated With Medication Refill Adherence in Cardiovascular-Related Diseases	Cohort study	Barriers to medication adherence were inadequate health literacy, sociodemographic backgrounds of patients, regimen complexity, and health status.	Level 3
Persell, Osborn, Richard, Skripkauskas, & Wolf 2007	Limited Health Literacy is a Barrier to Medication Reconciliation in Ambulatory Care.	In-person interview	Patients with inadequate health literacy in primary-care clinics were less likely to be able to name their AHM’s. Inability to name one's medications could increase the chance of medication errors or nonadherence.	Level 3
Schmid, Damush, Plue, Subramanian, Bakas, & Williams 2009	Current Blood Pressure Self-Management: A Qualitative Study	Cohort study	BP self-management included: external support, medication adherence, BP monitoring, lifestyle modification, and education for behavioral change to self-manage BP.	Level 3

Table 2

*Educational Content*

Authors	Title	Research Design	Results	Level of Evidence
Barnason, Zimmerman, & Young 2012	An Integrative Review of Interventions Promoting Self-Care of Patients With Heart Failure	Meta-analysis	Standard patient education augmented by cognitive-behavioral strategies enhanced patient's ability of self-care. Education increased medication knowledge and improved patients' confidence.	Level 1
Bosworth, Olsen, Grubber, Neary, Orr, Powers, & ... Oddone 2009	Two Self-Management Interventions to Improve Hypertension Control	RCT	Patient educated in home BP monitoring and lifestyle medication were associated with decreased systolic BP and diastolic BP.	Level 1
Conn, Hafdahl, Cooper, Ruppap, Mehr, & Russell 2009	Interventions to Improve Medication Adherence Among Older Adults: Meta-Analysis of Adherence Outcomes Among Randomized Controlled Trials.	Meta-analysis	Clearly and succinctly written instructions that educated patient in medications and patients' self monitoring of medication effects improved medication adherence.	Level 1
Crabtree, Stuart-Shor, & McAllister 2013	Home Blood Pressure Monitoring: An Integrated Review of the Literature	Meta-analysis	Beneficial outcomes resulted from home BP monitoring.	Level 1
Lee, Grace, & Taylor 2006	Effect of a Pharmacy Care Program on Medication Adherence and Persistence, Blood Pressure, and Low-	RCT	Educational interventions to teach patients drug names, indications, dosages, and adverse effects were associated with marked and sustained increase in medication adherence and	Level 1

Authors	Title	Research Design	Results	Level of Evidence
	Density Lipoprotein Cholesterol: A Randomized Controlled Trial		significant BP reduction.	
Magid, Ho, Olson, Brand, Welch, Snow, & ... Havranek 2011	A Multimodal Blood Pressure Control Intervention in 3 Healthcare Systems	RCT	Medication education improved medication adherence and BP control. Home BP monitoring also played an important role in BP control.	Level 1
Murray, Young, Hoke, Wanzhu, Weiner, Morrow, & ... Brater 2007	Pharmacist Intervention to Improve Medication Adherence in Heart Failure	RCT	Verbal instructions and written materials about medications for out-patients with heart failure improved adherence to cardiovascular medications. Written instructions were aimed at patients with low health literacy.	Level 1
Noureldin, Plake, Morrow, Tu, Wu, & Murray 2012	Effect of Health Literacy on Drug Adherence in Patients With Heart Failure	RCT	Patients with adequate health literacy had better adherence to cardiovascular drugs than those with inadequate health literacy. Written educational materials included drug therapy aimed at individuals with low health literacy levels. Simple language, short sentences, and well organized information in predictable sequence were used.	Level 1
Roumie, Elasy, Greevy, Griffin, Xulei, Stone, & ... Speroff 2006	Improving Blood Pressure Control Through Provider Education, Provider Alerts, and Patient Education	RCT	Patients who received both brief provider education and detailed patient education were able to achieve better BP control than patients who receive brief provider education alone. They were encouraged to adhere to AHM's and modify their	Level 1

Authors	Title	Research Design	Results	Level of Evidence
			lifestyle.	
Abdeesco 2012	Effectiveness of Health Instruction Related to Diet and Drug in Increasing the Level of Knowledge on Hypertensive Patients Associated With Cardiac Problems	Quasi-experiment	Increased knowledge in hypertensive patients were achieved by providing instructions about lifestyle modification, proper use of medication, and management of hypertension.	Level 2
Dawes, Kaczorowski, Swanson, Hickey, & Karwalajtys 2010	The Effect of a Patient Education Booklet and BP 'Tracker' on Knowledge About Hypertension. A Randomized Controlled Trial	RCT	Education regarding hypertension, target BP, and daily BP monitoring was associated with reduction of BP.	Level 2
Guirado, Ribera, Huergo, Borras, & Adiehta 2011	Knowledge and Adherence to Antihypertensive Therapy in Primary Care: Results of a Randomized Trial	RCT	Education regarding hypertension, AHM's, and adherence to medicine increased knowledge and adherence to AHM's. Instructions included mechanism of action, dosage, and adverse effects.	Level 2
Hacihasanoglu & Gözüüm 2011	The Effect of Patient Education and Home Monitoring on Medication Compliance, Hypertension Management, Healthy Lifestyle Behaviours and BMI in a Primary Health Care Setting	RCT	Systolic and diastolic BP was significantly reduced in patients who received education from nurses. Information conveyed the importance of medication adherence, effectiveness of the AHM's, side effects, action plans for side effects, and the importance of follow-up with PCP.	Level 2
Hill-Briggs, Renosky, Lazo, Bone, Hill,	Development and Pilot Evaluation of Literacy-Adapted	pre- and posttest with	Patients with very low educational backgrounds were able to achieve adequate	Level 2

Authors	Title	Research Design	Results	Level of Evidence
Levine, & ... Peyrot 2008	Diabetes and CVD Education in Urban, Diabetic African Americans	control	health literacy. Knowledge acquisition occurred regardless of literacy level.	

Table 3

*Format and Style of Educational Material*

Authors	Title	Research Design	Results	Level of Evidence
Katz, Jacobson, Veledar, & Kripalani 2006	Use of Pictorial Aids in Medication Instructions: A Review of the Literature	Meta-analysis	Patients gained better understanding of medication use when pictorial aids were used. Results were especially positive when pictures accompanied written or oral instructions.	Level 1
Negarandeh, Mahmoodi, Noktehdan, Heshmat, & Shakibaza-deh 2013	Teach Back and Pictorial Image Educational Strategies on Knowledge About Diabetes and Medication/Dietary Adherence Among Low Health Literate Patients With Type 2 Diabetes	RCT	Pictorial image and teach-back educational strategies increased knowledge and medication adherence in patients with limited health literacy. Teach back method verified patient's understanding.	Level 2
Gossell-Williams, Bennett, Dias, Foster, Houston, Wright & Fairclough 2012	Preference of Patient Information Leaflets Over Standard Drug Monographs by Patients Prescribed Hydrochlorothiazide, Nifedipine, and Enalapril	Pre- and posttest without control	Leaflets that provided simplified medication information were associated with improved knowledge. Leaflets contained medication use, dosage, common side effects, storage information, precautions, and signs and symptoms to report to PCP.	Level 2
Morrow, Weiner, Deer,	Improving Medication	RCT	Instruction sheets that best supported patient	Level 2

Authors	Title	Research Design	Results	Level of Evidence
Young, Dunn, McGuire, & Murray 2005	Knowledge Among Older Adults With Heart Failure: A Patient-Centered Approach to Instruction Design		comprehension and memory were designed to include large print and simple language. They improved medication knowledge in patients with low health literacy.	
Nurit, Bella, Gila, & Revital 2009	Evaluation of a Nursing Intervention Project to Promote Patient Medication Education	Pre- and posttest with control	Patients who received education leaflets in hospitals demonstrated increased knowledge. Each leaflet contained information about the drug indication, follow-up appointment, side effects, and when to seek medical advice.	Level 2
Morrow, Weiner, Deer, Young, M., Dunn, McGuire, & Murray 2004	Patient-Centered Instructions for Medications Prescribed for the Treatment of Heart Failure	Focus group	Patient-centered instructions should include medication name, purpose, dose, administration, warnings, and possible side effects. 12 to 14 point font, short, commonly used words, and simple sentence structure should be used.	Level 3
Center for Disease Control (CDC) 2009	Simply Put: A Guide for Creating Easy-to-Understand Materials	Expert opinions	Use simple terms and sentences. Avoid jargons and abbreviation. Give the most important information first. Create short lists (3-7 items) with bullets. Choose the best type of visual for instructional materials.	Level 4
Center for Healthcare Strategies 2005	Improving Print Communication to Promote Health Literacy	Expert opinions	Written materials should include plain and clear language with logical flow of information. Use clear headings and key points. Design should include bullet points, dark text on a light or white paper, large and familiar font. Graphics should clarify text.	Level 4

Authors	Title	Research Design	Results	Level of Evidence
DeWalt, Callahan, Hawk, Broucksou, Hink, Rudd, & Brach 2010	Health Literacy Universal Precautions Toolkit	Expert opinions	Key communication strategies include using plain, non-medical language, limiting content to 3-5 key points, repeating key points, encouraging patients to ask questions.	Level 4
Godzina 2011	What Impact Did You Make on Your Patients Today?	Expert opinions	Three main questions to ask patients: What were you told this medication is for? How were you told to take/use this medication? What were you told to expect when taking this medication?	Level 4

### Summary of Evidences

Dawes et al. (2010) identified three major areas of knowledge gaps among hypertensive adult patients. Of the three gaps identified, first was the need for the necessity of more than one drug—in combination with lifestyles modification—to control BP. Secondly, patients failed to understand that continued medication adherence was necessary to maintain BP. The third gap in knowledge was it could take up to six weeks for AHM's to reach therapeutic effect. Any effective educational method and instrument (aid) must therefore consider the above three gaps commonly found in patients' knowledge of AHM's.

The most frequently reported barrier to medication adherence was inadequate pharmacologic knowledge (Gazmararian et al., 2006). Sociodemographic variables such as age, ethnicity, gender, education, marital status, and social support also influenced medication adherence. Many adult patients reported inadequate knowledge of AHM's and BP self-management. Therefore, hypertensive adult patients needed to be educated

appropriately about their medications. Evidence suggested written and verbal instructions should focus on medication names, uses, common side effects, and signs and symptoms to report to healthcare providers. Evidence also pointed to the importance of instructing patients regarding daily BP monitoring at home, target BP, and the importance of follow-up with healthcare providers (Bosworth et al., 2009; Schmid et al., 2009; Dawes et al., 2010; Hacıhasanoğlu & Gözüm, 2011; Guirado, Ribera, Pacheco Huergo, Borrás, & Adiehta, 2011). To assist with this, patients could be provided with a BP tracker (see Appendix B).

The challenge, however, is complex ideas need to be communicated. Bosworth et al. (2009) found patients could easily understand information delivered by one nurse using a Flesch–Kincaid readability score of less than ninth grade. Hill-Briggs et al. (2008) suggested patients with very low literacy level ( $\leq$  fourth grade) benefited significantly from print handouts that met the criteria and strategies for low literacy health information. As noted above in Chapter 1, tools such as Flesch-Kincaid Readability could be used to ensure the language of the educational material does not exceed a certain educational level. Samples included in Appendix A fall at or below a fourth grade reading level.

In addition to readability and simplicity, other factors need to be considered. Format, style, and suitability of graphics are important factors (Hill Briggs, 2008). Educational material must be presented in simple and predictable sequences. Aesthetic factors should be subsumed under greater need for clarity and simplicity. Even fonts need to be measured since a large percentage of hypertensive adult patients are older. It was recommended printed material used 14–16 point font size, line length of less than 50

characters, organized with headers, subheaders, and bullet points (Hill-Briggs et al., 2008). Using graphics such as familiar objects and symbols and employing questions rather than simply describing information allow for effective communication of educational content (Hills-Briggs et al., 2008).

### **Grade A Recommendations**

The healthcare provider will provide verbal and written instructions while reviewing with patient medication information leaflets (level of evidence 1: Barnason et al., 2012; Conn et al., 2009; Lee et al., 2006; Murray et al., 2007; Noureldin et al., 2012; Roumie et al., 2006; level of Evidence 2: Abdeesco, 2012; Dawes et al., 2010; Hill-Briggs et al., 2008).

The healthcare provider will review the names of drugs, their use, anticipated side effects, and signs and symptoms of adverse effects to be reported to patient's primary care providers (level of evidence 1: Lee et al., 2006; Magid et al., 2011; Noureldin et al., 2012; level of evidence 2: Abdeesco, 2012; Guirado et al., 2011; Hacıhasanoğlu & Gözümlü, 2011; Nurit et al., 2009).

The healthcare provider will review personalized and patient-centered instructions, using simple, plain, non-medical language (level of evidence 1: Conn et al., 2009; level of evidence 2: Gossell-Williams et al., 2012; Morrow et al., 2005; level of evidence 3: Morrow et al., 2004; level of evidence 4: CDC, 2007; Center for Healthcare Strategies, 2005; DeWalt et al., 2010; Center for Healthcare Strategies, 2005). The healthcare provider should use language at fourth grade education level (level of evidence 2: Hill-Briggs et al., 2007).

The healthcare provider will instruct patient to measure and record BP in a BP tracker daily, and to bring BP tracker to follow-up appointment. The healthcare provider will provide patient with a copy of BP tracker (see Appendix B). The healthcare provider will review target BP, importance of regular medication adherence, and follow-up visits with PCP's (level of evidence 1: Bosworth et al., 2009; Crabtree et al., 2013; Magid et al., 2011; level of evidence 2: Hacıhasanoğlu & Gözüm, 2011, Dawes et al., 2010).

Along with written instructions in simple language, patients will benefit from relevant pictographs (level of evidence 1: Katz et al., 2006; level of evidence 2: Negarandeh et al., 2013).

### **Grade B Recommendations**

The healthcare provider will verify patient's medication knowledge by asking three questions:

- What is this medication for?
- How do you take this medication?
- What side effects are important to report to your doctor? (Level of evidence 2: Negarandeh et al., 2013; level 4: Godzina, 2011; CDC, 2007)

Educational materials should be designed to include 14 to 16 point fonts (level of evidence 2: Hill-Briggs et al., 2008; level of evidence 3: Morrow et al., 2005; Morrow et al., 2004; level of evidence 4; CDC, 2007).

Written instructions should be limited to five points and organized into a predictable sequence. For additional clarification, the healthcare provider should employ headers, subheads, and bullet points (level of evidence 2: Hill-Briggs et al., 2008; level of evidence 3: Morrow et al., 2004; level of evidence 4: CDC, 2007).

The healthcare provider will assess patient's barriers to medication adherence in terms of patient characteristics such as inadequate health literacy, health behaviors, and beliefs regarding health practice (level of Evidence 3: Gazmararian et al., 2006; Persell et al., 2007; Schmid et al., 2009).

The healthcare provider will invite questions by asking, what questions do you have? (Level of evidence 4: DeWalt et al., 2010; Center for Healthcare Strategies, 2005).

### **Grade C Recommendations**

The healthcare provider will repeat three key points: medication use, common side effects, and adverse effects to report (level of evidence 4: CDC, 2009).

## **Chapter 5: Discussion**

The present work represents evidence-based recommendations that converge on issues of patient education, medication adherence, and positive health outcomes for hypertensive adult patients. These recommendations promote patient wellbeing through increased knowledge of antihypertensive medications among adult patients with inadequate pharmacologic literacy. The project may have inadvertently neglected important considerations in regards to educating hypertensive adult patients toward achieving higher levels of medication adherence. We will return to this shortly, but let us briefly consider the implications of the recommendations made in this project.

### **Implications of Recommendations**

Healthcare providers play an important role in educating patients. In the area of medication adherence, it is the assertion of this project that we can overcome the challenges of limited time with patients, and ultimately educate even those patients with low levels of education. Based on evidence available, implementation of recommendations would help patients, especially those with inadequate pharmacologic literacy, to understand AHM's use, common adverse effects, and harmful adverse effects (Morrow, 2005; Hill-Briggs et al., 2008). This knowledge would ultimately lead to long-term positive outcomes for individual patients, as well as for other aspects of healthcare in the U.S.

Healthcare providers may follow the recommendations and utilize medication leaflets (See Appendix A) to provide verbal and written instructions pertaining to AHM's. In addition, healthcare providers may use Daily Blood Pressure Record (see Appendix B) to review patients' target BP, daily recording of BP, and the importance of

follow-up appointments. The recommendation and leaflets (see Appendix A) would promote patient understanding of AHM's during discharge from a hospital, primary care setting, and skilled nursing facility. When healthcare providers discuss benefits of medication adherence and daily home BP monitoring, patients are better educated to independently care for themselves and manage their hypertension. Prolonged uncontrolled hypertension has profoundly negative effects on target organ damage. Therefore, maintaining optimal BP can slow or prevent progression of target organ damage.

Another beneficial implication of the recommendations may be to empower patients toward self-care. For instance, armed with knowledge of AHM's and the ability to regularly monitor and their own BP at home, patients may become more motivated to check and record their daily BP in a BP tracker (Noureldin et al., 2012; Murray et al., 2007; Gazmararian et al., 2006). Furthermore, being aware of target BP, tracking their own BP may encourage patients to seek help when needed, reporting unusually low or high BP to their PCP's.

Of course, patients should be encouraged to follow up with their PCP's (Noureldin et al., 2012; Murray et al., 2007; Gazmararian et al. 2006). Patients' reports and follow-up appointments allow PCP's to assess severity of patient's symptoms, hypotension, and hypertension, then adjust medications or intervene accordingly. PCP's early detection and intervention of hypotension and hypertension can prevent worsening symptoms and hospitalization.

Implementing recommendations should result in development of standard protocol during discharge. The recommendations lead to a standardized protocol that

helps healthcare providers to clearly and succinctly impart their pharmacological knowledge to their patients. Currently, written discharge instructions in hospitals differ widely in their readability, layout, and designs. Standardized protocols can overcome educational barriers associated with readability of the instructions. Healthcare providers in hospitals may better serve their patient, if hospitals adopt and implement standardized protocols.

### **Limitations of Recommendations**

While the logic of presenting information in the simplest possible form has been made in Chapter 1, it must be acknowledged that complex ideas are often difficult to communicate fully without appealing to complex language. For example, this chapter of the project is at a Flesch-Kincaid readability grade level of 15.1, only readable to those halfway through undergraduate study. Simplifying information may inadvertently remove necessary components of that information. On the other hand, managing hypertension is far simpler task than describing how medication adherence and managing hypertension is achievable through sound educational principles.

Another limitation of the recommendations—and perhaps the entire project—arise from acceptance of time as limitation. Realities of U.S. healthcare system force providers to treat patients in limited time. Whether it is a busy nurse discharging a patient or a primary care provider seeing patients 15-minute increments, we have come to accept healthcare providers will interface with patients very briefly. Acceptance of present realities may simply be acquiescing to a broken system. However, it is outside the scope of this project to bring about systemic changes to the American healthcare system.

Finally, recommendations presented in this work suffer from not having been implemented and tested. While much of the distillation of information has been from experimental research already conducted, the entirety of the recommendations has not been tested in a practical clinical setting to validate the veracity of the claims made in this project. However, the evidence-based framework and model adopted in this work lend credibility to the recommendations made here. In addition, this limitation can be easily overcome, as suggested below.

### **Further Research and Practice**

Research in this project can be continued by implementing recommendations presented in this project in a clinical setting. Continued research will require cooperation of patients, hospital administrators, and approval from the IRB because the research will involve direct interaction with patients.

Also, studies cited in this work primarily focused on short-term retention of information. Further research is needed to improve education aimed at long-term retention of information and long-term medication adherence. Studies demonstrated patients could better understand and remember instructions in simplified, plain, non-medical language. These instructions increased immediate memory recall (Morrow, 2005). However, other studies suggested instructions might not increase long-term memory. Knowledge of AHM dissipated three months post-intervention. Sustained memory of medications might require constant intervention (Murray et al., 2007).

Evidence-based recommendations and medications leaflets will have to be reviewed and updated periodically to reflect the most current evidences related to medication education. As technology continues to develop, recommendations will also

need to include different types of media to educate patients; research is already being performed in this endeavor. For instance, a study titled, “The Personal Education Program: Next Generation,” sought to discover if web-based programs on tablets might help hypertensive adult patients in primary care settings with healthcare providers (Alicea-Planas, Neafsey, & Anderson, 2012).

While recommendations and informational leaflets presented in this project intend to help a broad spectrum of patients, the continuing increase of diversity in North America must be accountable in additional research. Extrapolations of data reported by the United States Census Bureau concluded ethnic and cultural diversity will continue to increase in the U.S. population (United States Census Bureau, 2011).

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## **Appendix A**

### **Medication Information Leaflets**

The following medication information leaflets were created according to the above recommendations. Instructions in leaflets were obtained from UpToDate (Brater, 2013) and Lexi-Comp Online (n.d.). In order to ensure patients with a fourth grade level education could comprehend instructions; this author used Flesch-Kincaid Readability to test reading level of the instructions. Pamphlets were designed to include 14 to 16 point fonts with simple sentences written in active voice. Multi-syllable words, medical jargon, and acronyms were avoided as much as possible. Instructions were limited to five points and organized into a predictable sequence. For additional clarification, leaflets use headers, subheads, and bullet points (Hill-Briggs et al., 2008; CDC, 2007). Standardized pictograms were used in pamphlets to convey important instructions (U. S. Pharmacopeial Conventions, 1997). They were intended to be particularly helpful in transferring important information to patients with lower reading levels (John et al., 2011; International Pharmaceutical Federation, 2009; CDC, 2007; Katz et al., 2006; IOM, 2004). When at home, patients can refer to written instructions for names, side effects, and signs and symptoms to report. Patients will be reminded to monitor blood pressure at home.

Healthcare providers may follow the recommendations and utilize medication leaflets (See Appendix A) to provide verbal and written instructions pertaining to the AHM's name, dosage, common side effects, and harmful adverse effects to report to their primary care providers. In addition, the healthcare providers may use Daily Blood Pressure Record (see Appendix B) to review patients' target BP, daily recording of BP,

and the importance of follow-up appointments.

## Diuretics

**Pronounced:** DI-yu-RET-iks

**Names:** chlorthalidone, chlorothiazide, hydrochlorothiazide, indapamide, metolazone, polythiazide, bumetanide, furosemide, torsemide, amiloride, eplerenone, spironolactone, triamterene



**Dose:** \_\_\_\_\_

### What are various uses of this drug?

- It is used to lower your blood pressure.
- They are sometimes called *water pills*.
- It is used to get rid of extra fluid.

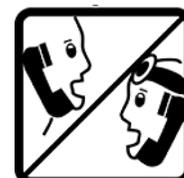


### What are common side effects?

- Increased need to go to the toilet.
- Feeling thirsty, dizzy, and weak.
- Low blood pressure. Rise slowly from lying or sitting to standing.
- High blood sugar. If you are diabetic, watch your blood sugar closely.
- Upset stomach.

### What are side effects you need to tell your doctor right away?

- Rashes, itchiness, swelling, fever, or tightness in chest and throat.
- Feeling very dizzy or passing out.
- Sudden change in eyesight, eye pain, or irritation.
- Unable to pass urine or change in the amount of urine passed.
- Muscle pain, weakness, or muscle cramps, or a heartbeat that does not feel normal.



### Reminder

Take this drug as ordered by your doctor. Keep your follow-up appointments with your doctor. Talk to your doctor about checking your blood work.

## Angiotensin Converting Enzyme Inhibitors

**Pronounced:** AN-ji-o-TEN-sen Kon-VERT-ing EN-zime in-HI-be-tors

**Names:** benazepril, captopril, enalapril, enalaprilat, fosinopril, lisinopril, quinapril, ramipril, trandolapril



**Dose:** \_\_\_\_\_

### What are various uses of this drug?

- It is used to treat high blood pressure.
- It is used to help your heart function after a heart attack.
- It is used to help a weak heart.

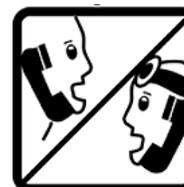


### What are common side effects?

- Feeling dizzy or weak.
- Low blood pressure. Rise slowly over a few minutes from lying or sitting to standing.
- Cough.
- Headache.

### What are side effects you need to tell your doctor right away?

- Rashes, itchiness, swelling, fever, or tightness in chest and throat.
- Feeling very dizzy or passing out.
- Cough that does not go away.
- A heartbeat that does not feel normal.
- Unable to pass urine or change in the amount of urine passed.
- Weight gain of 2 pounds in a day or 5 pounds in a week.



### Reminder

Take this drug as ordered by your doctor. Keep follow-up appointments with your doctor. Talk to your doctor about checking your blood work.

## Angiotensin Receptor Blockers

**Pronounced:** AN-ji-o-TEN-sen ree-SEP-ter BLOK-ers

**Names:** zilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan



**Dose:** \_\_\_\_\_

### What are various uses of this drug?

- It is used to treat high blood pressure.
- It is used to protect kidneys in diabetic patients.
- It is used to prevent strokes.



### What are common side effects?

- Feeling dizzy or weak.
- Low blood pressure. Rise slowly from lying or sitting to standing.
- High blood sugar. If you are diabetic, watch your blood sugar closely.
- Diarrhea.

### What are side effects you need to tell your doctor right away?

- Rashes, itchiness, swelling, fever, or tightness in chest and throat.
- Very bad headache, dizziness, or passing out.
- A burning, numbness, or tingling that is not normal.
- Unable to pass urine or change in the amount of urine passed.
- Change in strength on 1 side, trouble speaking or thinking, change in balance, or blurred eyesight.
- A heartbeat that does not feel normal.



### Reminder

Take this drug as ordered by your doctor. Keep follow-up appointments with your doctor. Talk to your doctor about checking your blood work.

## Beta-Blockers

**Pronounced:** BAY-ta BLOK-ers

**Names:** acebutolol, atenolol, beta blockers, beta-adrenergic receptor antagonists, betaxolol, bisoprolol, carvedilol, esmolol, labetalol, metipranolol, metoprolol, nadolol, oxprenolol, penbutolol, pindolol, propranolol, sotalol, timolol



**Dose:** \_\_\_\_\_

### What are various uses of this drug?

- It is used to treat high blood pressure.
- It is used to treat chest pain or pressure.
- It is used to help a weak heart.

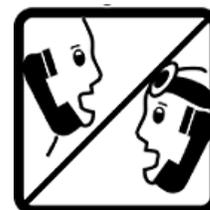


### What are common side effects?

- Feeling tired, dizzy, or weak.
- Low blood pressure. Rise slowly from lying or sitting to standing.
- Low blood sugar. If you are diabetic, watch your blood sugar closely.
- Unable to sleep.
- Dry mouth or eyes.

### What are side effects you need to tell your doctor right away?

- Rashes, itchiness, swelling, fever, tightness in chest and throat.
- Very bad dizziness or passing out.
- Feeling very tired or weak.
- Mood changes.
- Bluish color on skin the lips, nail beds, fingers, or toes.



### Reminder

Take this drug as ordered by your doctor. Keep follow-up appointments with your doctor. Talk to your doctor about checking your blood work.

## Calcium Channel Blockers

**Pronounced:** KAL-sem CHAN-nel BLOK-ers

**Names:** amlodipine, diltiazem, felodipine, nicardipine, nifedipine, nimodipine, nisoldipine, verapamil

**Dose:** \_\_\_\_\_



### What are various uses of this drug?

- It is used to treat high blood pressure.
- It is used to treat chest pain or pressure.

### What are common side effects?

- Dizziness.
- Feeling tired or weak.
- Flushing.
- Upset stomach.
- Belly pain.



### What are side effects you need to tell your doctor right away?

- Rashes, itchiness, swelling, fever, tightness in chest and throat, or trouble breathing.
- Very bad headache, dizziness, or passing out.
- Weight gain of 2 pounds in a day or 5 pounds in a week.
- A heartbeat that does not feel normal.
- Dark urine or yellow skin or eyes.
- Change in look of teeth or gums.



### Reminder

Take this drug as ordered by your doctor. Keep follow-up appointments with your doctor. Talk to your doctor about checking your blood work.

