TREATMENT DECISIONS FOR PEOPLE WITH LIFE LIMITING ILLNESSES: AN ANALYSIS OF TREATMENT VARIATION IN SECONDARY PREVENTIVE CARE FOR CARDIOVASCULAR DISEASE AMONG ELDERLY MEDICARE PATIENTS WITH DEMENTIA

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TREATMENT DECISIONS FOR PEOPLE WITH LIFE LIMITING ILLNESSES: AN ANALYSIS OF TREATMENT VARIATION IN SECONDARY PREVENTIVE CARE FOR CARDIOVASCULAR DISEASE AMONG ELDERLY MEDICARE PATIENTS WITH DEMENTIA

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This dissertation examines the effect of dementia on the treatment of coronary heart disease (CHD) in elderly Medicare beneficiaries. It specifically tests whether rates of utilization of evidence-based secondary preventive medication treatment (chemoprophylaxis) for CHD are different in patients with dementia compared to those without dementia. Data from the Cardiovascular Health Study were used to investigate the long-term effect of dementia on the use of four types of low burden and low risk chemoprophylaxis for CHD over time (ACE inhibitors, beta-blockers, lipoid-lowering medications and antiplatelet medications). The multivariate analyses employed a range of predictors including predisposing patient characteristics such as age, race, sex, education and the interaction of age and dementia status. Enabling variables included in the analyses are study site, income, supplemental insurance status, and residence in a nursing home. The care need variables include functional status, measured by activities of daily living, and comorbidites. The main findings reveal that the presence of any type of dementia, comorbid with CHD, has an effect on the use of beta-blockers and lipid-lowering medications. Additionally, patients with CHD and vascular type dementia are less likely to report taking beta-blockers, lipid-lowering medications, and antiplatelet medications, but more likely to report using ACE inhibitors. The results are mixed regarding the effect of timing of dementia onset of the use of chemoprophylaxis. Those who developed dementia before CHD were less likely to

report using a beta-blocker and lipid-lowering mediation, yet, those who developed dementia after CHD did not discontinue use of chemoprophylaxis after the onset of dementia. The results of this dissertation provide new empirical evidence of the difference in the rate of secondary chemoprophylaxis for CHD among elderly patients with dementia compared to those without dementia. Information about the effect of dementia on the treatment of CHD, as well as factors that predict utilization, could inform health policy to improve care for the millions of Americans living with dementia and CHD.

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Finally, this dissertation is dedicated to M. VonLunen and S. Makosky and the millions of people with dementia and their caregivers who struggle to make the best of each day in the face of an uncertain and unenviable future.

1.0 INTRODUCTION

This dissertation focuses on the effect of dementia on the treatment of coronary heart disease (CHD) in elderly Medicare beneficiaries. It specifically tests whether rates of utilization of evidence-based secondary preventive medication treatment (chemoprophylaxis) for CHD are different in patients with dementia compared to those without dementia. Although it does not test hypotheses about the causes of variation, this research does examine a range of potential factors and contributes to our understanding of the significant clinical, ethical, and policy implications of differences in utilization of health care services for patients with dementia and CHD. Section 1.1 includes a discussion of the unique characteristics of chronic illness in patients with dementia. Section 1.2 includes a summary of what we know about the impact of dementia on health services utilization, and section 1.3 discusses the factors that are hypothesized to affect the use of health services in patients with chronic illness and dementia. Section 1.4 presents the specific aims and the contribution of this research.

1.1 NONDEMENTIA ILLNESSES IN PATIENTS WITH DEMENTIA

Medical decision-making for older patients with multiple comorbidities is a difficult task. Often, there are competing risks for different conditions and the best available treatment for one may be constrained or even contradicted by another (Hoffman, 1996). Making treatment decisions for

patients with dementia and other comorbidities represents one of the most complex scenarios in medical decision making and is a potentially important area of inquiry for three reasons. First, dementia is unlike other chronic and progressive diseases that are eventually fatal because it attacks both a person's physical and mental capacities. Second, the progression of dementia is characterized by an extended period of deterioration that can last as long as a decade. Over the period of intellectual and physical decline, many opportunities arise for making medical decisions about everything from screening, to management of other non-dementia comorbidities, to treatment decisions at the end of life. The third potential importance of this work is based on the prevalence of dementia and the wide-ranging impact the disease has on individuals, families and the health care system.

1.1.1 Characteristics of dementia and their influence on the medical decision-making

Dementia is a disease that is characterized by a decline in memory and other cognitive functions. In many cases, loss of cognitive function can happen years before the physical body dies, leaving the person with end-stage dementia with very few of the characteristics that define personhood. Living with dementia is perceived by many people as living with low quality of life (Fried, 2002). The perception that people with dementia have poor quality of life is supported by the reality that a great majority of patients with dementia spend their final years in nursing homes, bed-bound, incontinent, and unable to recognize their family members (Post, 2000).

We believe that these perceptions about quality of life influence the medical decision-making process for patients with dementia and alter the choices about medical treatment that are offered by the physicians and accepted by patients and families. In particular, value judgments by the physician about the patient's present or future quality of life affect how physicians

analyze evidence (Eisenberg, 1979), present information to patients and families about treatment decisions (Pearlman, 1988), and how they use cues from families regarding treatment recommendations (Nelson, 1995).

1.1.2 Prolonged progression of dementia

The second potential importance of examining the effect of dementia on the treatment of comorbidities in general, and CHD in particular, is that dementia has a prolonged progression often spanning years, exposing patients to many other conditions that are common in older adults (Plassman, 2007). Epidemiological studies have estimated the overall median survival time from onset of dementia to death is 4.1 years for men and 4.6 years for women making it comparable to other terminal diseases that have longer progressions, such as class III heart failure and some malignancies (Xie, 2008; Larson, 2004). The extended period of life with dementia presents multiple opportunities for decision making about treatments. Physicians, patients and their families are faced with decisions than span the ranges of health services, from preventive screening to life-sustaining treatment.

The difference between dementia and other terminal diseases is that treatments that might otherwise be considered futile treatment for someone with shorter prognosis may be viewed more favorably for someone in the early stages of dementia. It is also true that treatment decisions made throughout the progression of dementia may alter the outcomes for patients and are likely to have a substantial impact upon the length or nature of the life to be lived.

1.1.3 Prevalence of dementia

The third potentially important implication of this research is that care of patients with CHD and dementia has a large impact on the health care system. It is estimated that 13.9% of people over age 71 have some form of dementia, comprising about 3.4 million individuals in the United States (Plassman, 2007). In an analysis using Medicare claims data, Maslow found that 30% of Medicare beneficiaries who had at least one claim with a dementia diagnosis also had a diagnosis of coronary heart disease (Maslow, 2002).Additionally, it is estimated that as many as 54% of dementia patients have had a myocardial infarction at some point in their life making them eligible for guideline-recommended chemoprophylaxis for CHD (Brauner, 2000).

1.2 EFFECT OF DEMENTIA ON HEALTH SERVICES UTILIZATION

Only a few studies have directly investigated the effect of dementia on the use of health services, and the findings from these studies vary. Some show that people with dementia have similar rates of utilization, especially for hospital and long-term care services (Weiner, 1998; Eaker, 2001). Other studies have produced results that show that people with dementia are less likely to use services, especially when the treatment is more invasive (Sloan, 2004; Gorin, 2004; Gupta, 2005). In some cases, utilizing health services at the same rate as those without dementia may be appropriate based on individual patient needs and goals of care. In other cases this may be a result of patients with dementia being exposed to care that is not beneficial and could be harmful.

Of the literature that has looked at the effect of dementia on treatment, five studies included patients with CHD and included guideline-recommended chemoprophylaxis as an

outcome. Sloan (2004) found that among patients hospitalized with acute myocardial infarction, those who had a diagnosis of dementia in their hospital chart were 50% less likely to receive invasive cardiac procedures than peers with no cognitive impairment. That study also reported that use of Angiotensin-Converting Enzyme (ACE) inhibitors during the hospital stay and at discharge was slightly lower for patients with a history of dementia, but that use of aspirin and beta-blockers was the same.

Other studies that have investigated the effect of dementia on treatment have included cardiovascular medications as a sub-class in the analyses. Hanlon (1996) and Schmader (1998) studied a community-dwelling cohort and found that overall use of prescription medications was lower for patients with dementia. Their results differed for cardiovascular medications as Hanlon found no difference in use and Schmader found lower use among those with dementia. Additionally, Schamader found that those with more severe impairment were less likely to use cardiovascular medications. Landi (1998) found similar results to Schmader in a study of medication use among nursing home residents. This study showed that after controlling for CHD, the more severe the dementia the less likely the resident was to be taking a cardiovascular medication.

These studies have various limitations. Sloan used medical record review to identify dementia diagnoses, which may have misclassified patients with respect to the presence of dementia, which would have led to underestimating the variation in chemoprophylaxis. Identifying dementia through medical charts alone or Medicare claims-based data has been shown to underestimate the prevalence of dementia by as much as 70% because these methods are likely to identify only people with advanced dementia or those who are admitted to the hospital from a long-term care facility (Taylor, 2002). The studies by Hanlon and Schmader

used a cohort of individuals from a five county area in North Carolina making the results difficult to apply broadly given that rates of chemoprophylaxis have been shown to vary by state and by region (Krumholz, 1998). The study by Landi only included nursing home residents with an official diagnosis of dementia and impairment severe enough to necessitate nursing home care making it difficult to apply to a community dwelling population.

Each of the studies are limited analytically in that they only employed cross-sectional analyses for patients with dementia. As a result, none are able to distinguish between the patients who developed CHD after their diagnosis of dementia from those with CHD who later developed dementia. We believe that it is possible that this distinction makes a sizable difference in treatment. The reasoning for this belief is that patients who experience symptoms of dementia first (memory loss, behavioral changes, dependence on others for activities of daily living, etc) may not consider initiating treatment for a new chronic condition if the treatment offers no direct benefit on quality of life or presents a new risk or burden.

This dissertation will overcome the methodological limitations of previous studies by using a cohort of people in which both CHD and dementia have been clinically validated. Additional information not available in previous studies also will be used, including a measure of severity of dementia, change in cognitive status over time, functional status, and the rate of secondary preventive treatments for CHD over a ten year time period. With a prospective cohort study, we are able to determine the sequence of developing dementia and CHD to evaluate whether the timing of the development of dementia plays a role in the treatment for CHD.

1.3 PREDICTORS OF HEALTH SERVICES UTILIZATION FOR PATIENTS WITH DEMENTIA

The studies described above that investigated the effect of dementia on use of health services found mixed results. None investigated potential causes that might be influencing patterns of utilization for patients with dementia. We believe that these findings may be the result of both physician-related predictors and individual patient characteristics that predict use. While the empirical analyses in this dissertation investigate utilization of chemoprophylaxis for CHD, the discussion surrounding this research includes possible predictors of use. Two conceptual models are used to organize the discussion. They include a conceptual model proposed by Eddy (1990) for evidence-based medical decision-making and the model designed by Andersen (1995) to understand patient characteristics that influence the use of health services. The Eddy model includes elements such as analysis of evidence, and judgments about the evidence and its application to the patient. This model is used to frame the discussion regarding physician-related factors that may influence utilization of health services, in general, and chemoprophylaxis for CHD in particular, for people with dementia. The predictive factors discussed here and in following chapters include how physicians analyze and apply evidence in medical decision-making and the role of their subjective judgments about the patient's quality of life.

The Andersen model of health services utilization is used in this research to inform and organize patient-level predictors that may impact use of chemoprophylaxis for patients with CHD and dementia. Elements of the model include predisposing factors, such as age, sex, and race, enabling factors such as access to health care and income, and care need factors that account for a patient's health care needs as defined by their functional and cognitive status, comorbidites, and their perceived need for care.

1.3.1 Physician-related predictors of health services utilization for patients with dementia

The first physician-related predictor is variation in geographic practice patterns. Research on variation in health care utilization has found differences for a variety of different types of health care services across different geographic regions (Wennberg, 2004, Fischer, 2003). In some cases, these differences reflect the extent to which medicine lacks a firm evidentiary base for treatments. When the evidence base is strong, treatment differences tend to be much smaller (although the impact of new evidence is often disappointingly small). The push to develop more "evidence-based guidelines" for treatment grows out of these findings. From this perspective, greater uniformity in chemoprophylaxis for patients with dementia would, in general, be desirable, although it is often unclear how to incorporate competing risks of treatment and patient's goals for care. In the case of secondary prevention for CHD, systematic application of the best evidence for chemoprophylaxis has been shown to improve outcomes (MI and death) (Smith, 2001), reduce geographic treatment variability (Chassin, 1987), and potentially, improve overall quality across the entire health care system (Fischer, 2003). Because no medical recommendations exist for treating CHD for patients with dementia, those with both diseases are likely be treated the same as those with only CHD.

The second physician-related predictor includes the use of clinical information about dementia that may predict how physicians analyze and apply evidence to treat comorbidities in people with dementia. For example, it is known that patients with dementia have a shorter life expectancy than their age-matched peers without dementia (Larson, 2004). This is relevant to the medical-decision process in that if a patient is not expected to live long enough to achieve benefit from a particular treatment, it may not be presented to them as an option. This was demonstrated

in a study by Marwill (1996) that found lower rates of guideline-recommended breast cancer screening for older women with dementia.

Third, physicians may have a heightened sense of therapeutic caution based on the increased risk of a treatment, especially for more invasive procedures that may be perceived by patients with dementia as an assault if they have little insight into the purpose or intention of the treatment (Rango, 1985). Although subtle, even less invasive treatments, such as medications for people with dementia, may have a different risk-benefit ratio given potential issues with patient adherence and their inability to recognize or report serious side effects (Brauner, 2000).

The fourth physician-related predictor is the subjective influences on the medical decision-making process. These include judgments by the physician regarding a patient's quality of life or social worth. Perceptions that a patient's quality of life is poor or will shortly become poor due to dementia may result in less aggressive treatment for comorbidities. The influence of this predictor is consistent with previous research that has shown the influence of physicians' personal perceptions and judgments about a patient on the medical decision-making process and on treatment outcomes (Ubachs-Moust, 2008; Brock, 1993). Research done by Crane (1975 that asked physicians to recommend medical treatments for hypothetical cases found that when the patient has irreversible mental disability as compared to physical disability, they were less aggressive in their treatment recommendations.

1.3.2 Patient-related predictors of health services utilization for patients with dementia

The second conceptual model used in this research is the Andersen model of health services utilization (Andersen, 1995). This model presents the ideal framework for organizing the discussion about the role of individual patient and social level correlates that may predict

utilization of chemoprophylaxis for CHD among patients with dementia. This model was originally created to explain the use of formal health services such as hospital care, but has been adapted and applied to predict and explain the use of other types of health services, including medication (Sleath, 2004) and long-term care (Bradley, 2002). It was selected for the research in this dissertation because its framework acknowledges the importance of the external environment as well as the individual patient and family characteristics.

The relevance of patient level predictors on the use of chemoprophylaxis for CHD among those with dementia is that differences in the use of a variety of health care services have been observed across a number of individual characteristics such as age, race, sex, and insurance coverage (Gornick, 1996; Federman, 2001). Additionally, we believe that for patients with dementia and CHD, observed differences in the use of health services can also manifest from a patient's own knowledge, attitudes, beliefs and judgments about their disease and quality of life. The parallel predictor of the physician's perception of quality of life is that of the patient's own perception of their quality of life as a predictor of use. For example, a patient may be less likely to accept or adhere to a treatment if they perceive their current or future quality of life as poor (Fried, 2002). This influence may likely be extended to the knowledge, attitudes, beliefs and judgments of the family member about the patient given the impact of dementia on decision-making and the role of the family in medical decision-making (Nelson, 1995). Although it is reasonable to assume that even if the patient is able to participate in the decision-making process, they are part of a family that has a set of collective goals, purposes and interests for all of its members, so few decisions are ever made individually. Given this, unless otherwise noted, patient and family knowledge, attitudes, beliefs and judgments are collectively considered,

although a section in Chapter 2 will discuss the literature on the differences between patient preferences and their preferences as perceived by family members.

1.4 CONTRIBUTION OF THIS RESEARCH

This dissertation will test differences in low burden, low risk evidence-based secondary preventive medication treatments for CHD between those with dementia and those without dementia. Additionally, these medications are low cost from a societal perspective. We expect to find smaller differences for medications than might be found for more intensive life-extending interventions or expensive treatments for CHD such as bypass surgery. We also might expect to find a bigger difference for preventive screening procedures such as mammography and colonoscopy, where even those with mild dementia would be unlikely to live long enough to achieve any benefit from screening (Braithwaite, 2007; Holmes, 2006).

This dissertation research is the first to examine the long-term effect of dementia on the use of low burden and low risk chemoprophylaxis for CHD. The results of this dissertation will provide new empirical evidence of the difference in the rate of secondary chemoprophylaxis for CHD among elderly patients with dementia compared to those without dementia. Information about the effect of dementia on the treatment of CHD, as well as factors that predict utilization, could inform health policy to improve care for the millions of Americans living with dementia and other conditions.

The empirical analyses in this research compare self-reported use of chemoprophylaxis for two distinct groups of community-dwelling Medicare beneficiaries over a ten year period; those who only develop CHD and those who develop both CHD and dementia during the study

period. Among the sample with both diseases, there are two sub-samples: (1) those who develop dementia before CHD and (2) those who develop dementia after CHD. The three specific research questions in this dissertation are:

1. Are Medicare beneficiaries with dementia *and* coronary heart disease (CHD) less likely to use guideline-recommended medications for the secondary prevention of CHD compared to those with CHD only?

We predict that after controlling for confounding factors, people with dementia will be less likely to report using chemoprophylaxis for CHD because the co-morbidity of dementia will have a negative effect on the treatment.

2. Are Medicare beneficiaries who develop dementia *before* CHD less likely to use guideline-recommended medications for the secondary prevention of CHD compared to those who develop dementia *after* CHD?

We hypothesize that the order of the disease development is an important predictor in the use of chemoprophylaxis given that physicians and families may find it harder to reduce or stop treatment for an existing co-morbidity compared to initiating a new treatment for a new disease. Thus, we predict that patients who develop dementia first will have lower rates of utilization compare to those who developed CHD first.

3. Are Medicare beneficiaries who develop dementia *after* they develop CHD more likely to discontinue guideline recommended medications for the secondary prevention of CHD after they develop dementia?

We hypothesize that some people who have CHD and are taking chemoprophylaxis will discontinue the use of medications after the development of dementia. We predict that although the rate of use may be higher than those who develop dementia first and never start the medications, those who develop dementia after CHD will be more likely to discontinue medications for the secondary prevention of CHD.

2.0 LITERATURE REVIEW

The literature reviewed for this dissertation is organized into four sections. Section 2.1 is a summary of the evidence-base for the four subclasses of cardiovascular medication that are guideline-recommended for the secondary prevention of CHD. Section 2.2 provides an overview of the Eddy model for evidence-based medical decision making by physicians and describes the elements of the model based on their potential contribution to variation in the use of chemoprophylaxis for people with CHD and dementia. Section 2.3 includes a description of the Andersen model of health services utilization. The findings from the literature in this section are organized around the elements of the Andersen model that we predict contribute to the variation in the use of chemoprophylaxis for people with dementia and CHD. Although these two models were created to explain different constructs (physician decision making and predictors of health services utilization, respectively), each model contains elements that are relevant to the exploration of the effect of dementia on the use of chemoprophylaxis for CHD. Section 2.4 introduces a modified conceptual framework that combines elements from both the Eddy and Andersen models and includes a summary of the literature that directly looks at the effect of dementia on differences in health services utilization for older adults.

2.1 SECONDARY CHEMOPREVENTION OF CHD IN OLDER ADULTS: A SUMMARY OF THE EVIDENCE

Coronary heart disease (CHD), also called ischemic heart disease (IHD), coronary artery disease (CAD), or coronary atherosclerosis is one of the most common chronic conditions among older Medicare beneficiaries (American Heart Association, 2004). Coronary atherosclerosis is the hardening and narrowing of the coronary arteries that supply the blood that carries oxygen and nutrients to the heart muscle. When coronary arteries are narrowed or blocked by atherosclerosis, adequate amounts of blood flow to the heart muscle are compromised. Disease caused by the lack of blood supply to heart muscle is called coronary heart disease. Coronary heart disease includes myocardial infarction, sudden unexpected death, stable and unstable angina pectoris, abnormal heart rhythms, and heart failure due to weakening of the heart muscle. It is estimated that 19% of all Medicare beneficiaries aged 65 to 74 have CHD and among those 75 and older, 25% have prevalent CHD (American Heart Association, 2004), making them eligible for secondary preventive treatment.

The pharmacological management and secondary prevention of CHD has been revolutionized in the past few decades as a result of more patients surviving initial myocardial infarction (MI) events. Evidence for the use of medications that preserve heart function, stabilize plaque in the arteries, and prevent recurrent atherothrombotic events continues to grow. Several subclasses of cardiovascular medications have undergone rigorous evaluation in large, randomized, controlled trials (RCTs) and have been designed to improve the clinical features of CHD as well as outcomes after an MI. While most of these “gold standard” RCTs have specifically excluded older adults with dementia, the evidence generated serves as the basis for

how physicians should effectively treat and manage patients with CHD, despite the presence of other comorbidities.

The four subclasses of cardiovascular medications selected as dependent variables for this research include those with the strongest evidence of reducing mortality from CHD following an MI. This evidence serves as the basis for the recommendations put forth in clinical practice guidelines (CPGs) regarding the treatment and management of patients following an MI. These CPGs emphasize the early initiation and continued use of angiotensin-converting enzyme inhibitors (ACE inhibitors); beta-adrenergic blocking agents (beta-blockers); HMG-CoA reductase inhibitors (lipid-lowering medications [statins and non-statins]); antiplatelet medications such as cyclooxygenase inhibitors (aspirin); and adenosine diphosphate (ADP) receptor inhibitors (such as Plavix®) (Giugliano & Braunwald, 2004; Pollack & Gibler, 2001; Smith, 2001; Ryan ., 1996; Hunt, 2005). Sections 2.1.1 to 2.1.4 present a brief summary of the evidence for each of these medications, and focuses, when that information is available, on the evidence of effectiveness in older adults. No results include information about effectiveness of these medications for patients with dementia. Given the lack of evidence, it is assumed, for the purposes of this research, that these medications are equally effective in people with dementia in the secondary prevention of CHD.

2.1.1 ACE inhibitors

The results of well-conducted, randomized, controlled clinical trials on the effectiveness of ACE inhibitors in reducing mortality following an MI have been so consistent and so conclusive that much of the recent literature emphasizes implementation rather than research. For example, the results of a comprehensive meta-analysis of 32 randomized trials, including a total of 7,105

patients, showed that ACE inhibitors significantly reduced mortality by 23% in patients following an MI (Garg, 1995). Studies such as the Heart Outcomes Prevention Evaluation Study (Yusuf, 2000) have shown that in a cohort of 5,069 persons ≥65 years of age, 4 years use of ACE inhibitors decreased the incidence of subsequent MIs by 22%. The conclusion of most of the large trials is that unless systolic blood pressure is <100 mm Hg, ACE inhibitors should be initiated within 24 hours of an MI and continued indefinitely, since benefits have been shown to persist years after an MI (Flather, 1995; Pfeffer, 1997).

2.1.2 Beta-blockers

The role of beta-blockers in the treatment and management of patients post-MI is well established (Yusuf, 1985). The beneficial effects result from decreasing heart rate, blood pressure, myocardial oxygen demand, and arrhythmogenesis (Park, 1995). In aggregate, the data suggest that beta-blocker use reduces nonfatal MI by approximately 25%, which is paralleled by a 25% reduction in the mortality rate. A retrospective study of Medicare beneficiaries in New Jersey from 1987 to 1992 found that people ≥65 years who were treated with beta-blockers after an MI had a 43% decrease in 2-year mortality and a 22% decrease in 2-year cardiac related hospital readmissions. These results were in comparison to an age-matched cohort who were not treated with beta-blockers (Chadda, 1986). One of the largest trials on the effectiveness of beta-blockers following an MI, the Beta-Blocker Heart Attack Trial (BHAT), found that any reduction in mortality holds for up to 3 years following an MI (Soumeri, 1997). The ACC/AHA guidelines recommend that all patients without clear contraindications (hypotension, sinus bradycardia, partial atrioventicular blockage, etc.) should receive beta-blocker therapy within a few hours of an MI and continue them indefinitely (Smith, 2001).

2.1.3 Lipid-lowering medications

Lipid-lowering medications are strongly indicated for use as secondary prevention after acute MI, for those with and without elevated cholesterol. The Cholesterol and Recurrent Events (CARE) trial demonstrated that a statin lipid-lowering medication, compared with placebo, reduced the rate of death or MI in patients with previous MI by 24% (95% CI, 9% to 36%) over a 5-year follow-up (Sacks, 1996). In a study of 1,238 older adults aged 65–75, those treated with the lipid-lowering medication pravastatin had a 45% reduction in death and a 32% reduction of other major coronary events compared to those treated with a placebo 5 years following their initial MI (Lewis, 1998). No studies to date have produced positive results of the efficacy of administering lipid-lowering medications immediately after an MI, as all data are based on longer-term efficacy and follow-up post-MI. Evidence of the effectiveness of long-term treatment is of particular relevance when considering application of the data to patients with dementia. Given the shortened life expectancy of patients with dementia, it is likely that the benefits of lipid-lowering mediations may not be realized for dementia patients. For example, a study by Collins (2003) found that treatment with a statin may not be effective at reducing cardiovascular events until 5 years of treatment.

2.1.4 Antiplatelet medications

Based on years of evidence, ACC/AHA guidelines recommend the use of aspirin for an indefinite period of time following an MI, unless there is some contraindication to its use. Randomized trials involving 20,006 patients have shown that aspirin and other antiplatelet drugs administered to patients after an MI decreased the incidence of recurrent MI by 36 deaths per

1,000 patients treated for a 2-year period (Antithrombotic Trialists' Collaboration, 2002). These benefits were found to be irrespective of age, sex, blood pressure, or history of diabetes. The most comprehensive and concise source of data about the effect of antiplatelets for the secondary prevention of CHD is the Antiplatelet Trialists' Collaboration (1988). This meta-analysis of 172 randomized trials conclusively demonstrated the value of aspirin use after an MI (4% relative risk reduction of MI found between years 1 and 3 post-MI). Studies of other antiplatelet medications, clopidogrel in particular, have shown an overall 8.7% relative risk reduction of mortality compared to aspirin after 1.9 years of follow-up (CAPRIE, 1996).

While the evidence base is strong regarding the effectiveness of these medications in reducing subsequent MIs and cardiovascular related mortality, none of the studies cited above included patients with dementia. Unless life expectancy is compromised by some other non-CHD factor, hence affecting the time until benefit, it can be assumed that those with dementia would experience the same secondary preventive benefits as cited in the studies.

2.2 ANATOMY OF A MEDICAL DECISION

The analytical goal of this dissertation is to explore the effect of dementia on the use of evidence-based chemoprophylaxis for CHD. The evidence summarized above is from RCTs that exclude patients with other comorbidities. This evidence is often what informs the creation of physician decision aids, such as clinical practice guidelines. Given this, these guidelines are often "blunt" and provide no suggestions on how to individualize the recommendations based on relevant clinical factors such as comorbidities that affect life expectancy or increased risk of adverse event (Braithwaite, 2007; Walter, 2001; Roberts, 2009).

Additionally, guidelines rarely address the contribution of personal patient factors in the medical decision-making process about treatment, such as patient preferences and goals of care (Boyd, 2005). In a conceptual framework developed by Eddy (1990), Eddy describes the components that physicians use to make evidence-based medical decisions. The model considers (1) analysis of the evidence and (2) value judgments as primary ingredients. The inputs into the process include: (a) evidence, (b) the physician's scientific judgments about the evidence, and (c) preferences of all parties involved. In the case of decision making for patients with dementia, this would include the physician, patient, and patient's family. Outcomes of the process include how the evidence is presented to the patient and then the final treatment decision. Figure 2.1 provides a graphical representation of the framework.

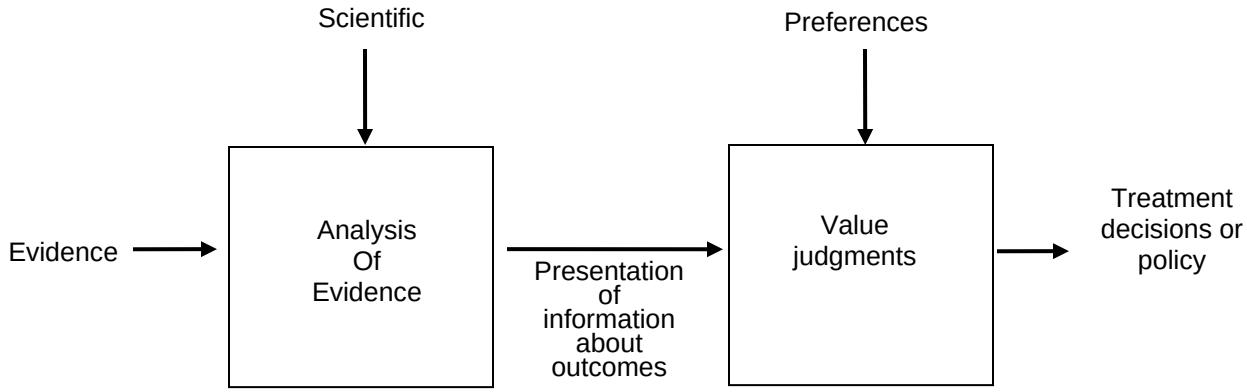


Figure 2.1 Components of an Evidence-based Medical Decision.

In some respects, this model is ideal for examining the effect of dementia on medical decision making for chemoprophylaxis because it acknowledges both the use and the interpretation of scientific evidence as well physician value judgments about the patient. Evidence from the literature, summarized below, supports the theory that physician judgments about a patient may affect their treatment decisions (Crane, 1975; Ubachs-Moust, 2008; Marwill, 1996). Applying

the Eddy model to this dissertation research involves first gathering and reviewing the evidence for the treatment and management of CHD. This step shapes what and how evidence about potential treatments is presented to the patient. The second step involves the incorporation of personal value judgments of the patient, family, and physician. This mix of value judgments may likely include very different concerns about such things as the amount of burden to impose on a patient with dementia (Walter, 2001), judgments about the marginal benefit of care (Raik, 2004; Holmes, 2006; Post, 2000; Brauner, 2000), and judgments by the physician, and potentially the family, about the diminished social worth of people with dementia (Callahan, 1992; Crane, 1975). While the Eddy model does not focus on the distinct difference between the preferences and values of the patient, family, and physicians and their effect on the final decision about how best to treat, Section 2.2.1 expands these elements of the model by focusing the discussion on how they might differ and their impact on use of health services.

2.2.1 Analysis of the evidence

The Eddy model presents medical decision making as a linear process that begins with review and analysis of the best available data. The evidence originates from the best available external evidence that is clinically relevant research that is scientifically sound and can be used to evaluate the consequences or outcomes of each of the potential treatment. Findings from the literature on variation of health services have shown that when there are differences in the degree of evidence and high levels of uncertainty about the effectiveness of a treatment or procedure variation in treatment is greater (McPherson, 1982; Wennberg, 1982).

Evidence also is generated and analyzed based on the individual clinical expertise of the physician (Sackett, 1996). Since outcomes associated with different treatments may be

conflicting, Eddy believes that this step should involve principles and methods to ensure that, to the greatest extent possible, population-based policies and individual medical decisions are consistent with evidence of effectiveness and benefit. Presumably the physician considers whether the evidence supports a conclusion to determine if treatment "X" is more effective than treatment "Y" in improving survival. Other important health outcomes such as risks and side effects are also evaluated. Using lipid-lowering medications as an example, in the analysis of the evidence stage in the Eddy model, would include the effectiveness data about the benefits of long-term statin use in reducing subsequent MIs as well as data on the time until benefit and the realizable benefit that a statin can provide someone with a limited life expectancy.

When the evidence is synthesized into decision aids that are intended to help physicians analyze the evidence, such as clinical practice guidelines, it is important to note that at some level, value judgments about the evidence itself are made, for example, which study results to consider and what is considered the threshold for effectiveness (Tunis, 2007; Eddy, 1990).

2.2.1.1 Clinical practice guidelines for CHD

The most common sources of summarized and organized evidence are in the form of consensus statements or clinical practice guidelines (Woolf, 1993). Clinical practice guidelines (CPGs) are defined as systematically developed statements that integrate the best research evidence with clinical expertise. Their purpose is to assist physicians in systematically applying the evidence when making decisions on how best to treat a particular patient. It is important to note, however, as discussed above, that in the context of "evidence and values" as part of the medical decision-making process, determining what evidence to use in establishing a clinical practice guideline introduces subjectivity into the interpretation and translation of the evidence.

The most cited CPG for the treatment of CHD with MI and angina is from the American College of Cardiology/American Heart Association (Smith, 2001). As noted above, this guideline recommends for all patients, unless contraindicated, the use of secondary chemoprevention with platelet-inhibitors, beta-blockers, lipid-lowering mediation, and angiotensin-converting enzyme inhibitors (Hunt, 2005; Smith, 2001).

Not unlike guidelines for other diseases, the ACC/AHA guideline does not address dementia as a condition that may be comorbid with CHD, nor does it provide guidance on how to adjust the recommendations for someone with dementia. Some guidelines make relevant adjustments based on morbidity and mortality and consider the time-until-benefit for a treatment for people with a limited life expectancy (Holmes, 2006), but most are "blunt" and not consider how a patient's goals of care may adjust the recommendation (Boyd, 2005; Mast, 2000). These missing components may make it especially difficult for physicians to apply them to patients with dementia and can even put patients at risk of receiving inappropriate treatments or treatments that are inconsistent with their goals (Walter, 2004).

While guidelines originated as a way for physicians to easily apply the evidence in real-time medical decision making, they are increasingly being used in health policy initiatives to measure and reward quality of care. Programs such as pay-for-performance (P4P) programs that financially reward adherence to guidelines may have an impact on chemoprophylaxis for patients with dementia. The positive effect of these programs may be that patients with dementia, who were at risk of under-treatment owing to value judgments by the physician, may now be treated similarly to those without dementia. On the other hand, a negative consequence may be that those with CHD and dementia would be put at risk of excessive and inappropriate treatment that does not align with their goals. Although not a central theme of this research, it is important to

consider that using CPGs to measure quality within the health care system may create a conflict of interest in the treatment of patients if the quality indicators being used do not account for the unique and complex needs and preferences of patients with dementia (Boyd, 2005).

2.2.2 Value judgments

It seems intuitive that medical decisions should be informed by the best available scientific evidence, as outlined in step 1 of the Eddy model. However, it is important to consider the framing of evidence when applying it to a clinical decision. A procedure with a demonstrated advantage by one metric may not be the best choice for all patients and in all circumstances. In the Eddy model, the first step of the decision-making process is the "evidence-based medicine" phase. The second step in the process involves additional factors that are used to judge the best treatment for a particular patient. While much of the literature on evidence-based medical decision making mistakenly assumes that decisions are free of value judgments, value judgments made by the physician naturally play a part in the decision-making process (Eisenberg, 1979).

Medical decision making for people with dementia is especially susceptible to the influences of value judgments given that dementia often provokes moral questions about quality of life, social worth, and even the meaning of life, given its progressive attack on both mental and physical abilities. These judgments affect the interpretation of the evidence when weighing the benefits, harms, and costs of a treatment (Eddy, 1990). In the model, evidence about the consequences of the treatments is examined alongside patient preferences, values, and beliefs; family preferences, values, and beliefs; and physician values and beliefs. For patients with dementia this step in the process includes relevant clinical judgments about problems of adherence to medications, communication issues that may affect a person's ability to report

adverse effects, the ability of the patient to appreciate the reason for the treatment, and the patient's capacity to make an informed choice about treatment. Additional value judgments that raise ethical issues surrounding the treatment of people with dementia may include physician perceptions about the patient's quality of life (Uhlmann, 1988) as well as family members' perception of the patient's quality of life. The following sections (2.2.2.1 and 2.2.2.2) review the literature on the role of patient and family preferences and physician value judgments as it relates to medical decision making for people with dementia.

2.2.2.1 Patient preferences in medical decision making

In medical decision making, the term patient preferences has two different definitions. The first is the patient's preferred choice of treatment based on his or her values and beliefs. The second is the patient's preferred degree of involvement in the decision-making process. Both definitions are relevant for the discussion regarding the role of preferences in medical decision making for patients with dementia. First, patients with dementia, like all patients, have values and beliefs that shape their preferences for care. Second, the etiology and inevitable progression of the dementia requires that others (physicians, family, or other surrogates) take an active role in making decisions about medical care. The following sections address both aspects of patient preferences in the decision-making process and how they might contribute to predicting the use of chemoprophylaxis for CHD.

Patient preferences are the manifestation of individual and familial values and beliefs about medical care and treatments. The plurality of preferences have been cited as a potential sources of variation in the utilization of health care services, especially for treatments that have uncertain evidence about the ratio of harm to benefit, or the potential options are sensitive to the value that patients place on benefits and harms (Wennberg, 1982).

Honoring patient preferences for treatment is based on the ethical principle of patient autonomy and the belief that people have a right to control what happens to their body (Beauchamp, 2008). For many decades the dominant approach to making decisions about treatment, especially for those with compromised cognition, has been one of paternalism. In recent years this model has been challenged by doctors, patients, medical ethicists, and researchers who advocate different models between doctors and patients such as shared treatment decision making (Charles, 1997). Through a process such as shared decision making (Charles, 1997) patient autonomy is promoted by a two-way exchange of information that includes the solicitation of patient preferences.

For patients who cannot actively participate in the decision-making process or communicate their preferences, advance directive documents have been presented as a tool that can be used to convey information about specific treatment preferences. There is disagreement in the literature on the usefulness of advance directives or prior discussions for guiding decision making. For example, a study on the use of advance directives found that many individuals prefer to express general preferences (e.g., values, goals for care) rather than document specific medical treatment preferences (Hawkins, 2005).

Other research about the usefulness of advance directives in providing information about preferences suggests that eliciting patient preferences in advance of care is limited, since patients' preferences about treatment options often change when faced with a particular decision and are dependent on the outcomes of the potential treatments (Fried, 2002). In a study of 226 people aged ≥60 years who had a limited life expectancy due to cancer, congestive heart failure, or chronic obstructive pulmonary disease, participants were asked to describe preferences for treatment under certain scenarios. The first scenario would be whether they would want to

receive a particular treatment if the outcome was known with certainty, but had different likelihoods of adverse outcomes. The outcome without treatment was death. Nearly all participants (98.7%) chose treatment if the burden of treatment (i.e., length of hospital stay, extent of testing, and invasiveness of intervention) was low and the outcome was restoration of current health. If treatment burden was high, 11.2% of the sample did not want treatment even if their current state of health could be restored with the treatment. If the outcome of the treatment changed and resulted in severe physical impairment, despite the low burden of the treatment, 74.4% of the sample did not want treatment. If the outcome of the treatment was severe cognitive impairment, 88.8% of the sample did not want treatment, even if the treatment was low burden. Cognitive impairment was described as the participant being unaware of his or her surroundings and unable to recognize family members.

The findings from this study are particularly relevant to the discussion of the role of patient preferences in treating CHD in people with dementia. For example, asking patients with dementia their preference for managing their CHD and preventing another MI, after they have already experienced an MI or angina, would require information about the possible outcomes for treatment vs. no treatment. While chemoprophylaxis for CHD is low burden (i.e., medications are taken orally and have few side effects) and reduces the likelihood of another MI or death from CHD, it may potentially increase the likelihood of living longer with dementia and experiencing more of its effects and dying of its complications.

A second relevant finding from the Fried study is that patients in the study sample were already older and already had a serious life-threatening illness. Despite this, 88.8% said that they would refuse even a low-burden treatment if the outcome was cognitive impairment. While an outcome of chemoprophylaxis is not cognitive impairment for patients who already have

dementia, treating CHD may likely extend their experience with dementia by warding off a more sudden death from an MI or cardiac event. These types of trade-offs are likely important aspects of patient preferences but are rarely cited in the literature as something to consider in the medical decision-making process.

In the Eddy model, patient preferences for health care impact the application of the evidence by imposing different priorities for outcomes. For example, if the evidence for treatment "Y" shows that mortality is lowest but the burden of treatment is high and quality of life following the treatment is altered owing an effect on mobility, it is conceivable that someone with moderate dementia who is still able to ambulate independently would not prefer this option. This example highlights that medical decision making for people with dementia and CHD requires weighing the evidence in different scenarios, including the scenario of not treating the CHD, and the impact on important outcomes relative to values and beliefs such as length of life, quality of life, and implications for the patient and the family regarding long-term care needs.

An alternative definition of "patient preferences" in medical decision making refers to the patient's preferred degree of involvement in the process. For patients with dementia, there is a high level of certainly that at some point during the disease progression other people will need be involved in decision making. In most cases, others are family members. It is also true that the outcomes of particular treatment decisions will have an impact on the family given their extensive role in care giving (Ory, 1999). Some patients with dementia may never choose an active role in medical decision making and defer all decisions about treatment to medical professionals or family members even when they are still cognitively able to participate. Others, when still able, may take an active role and participate in shared decision making with their physician, with or without involvement from family. Despite the different levels of potential

participation, virtually all patients with dementia, unless they die in an earlier stage of cognitive decline, will require others to represent their preferences in the decision-making process.

Reference to "patient preferences" in the dementia literature often includes a discussion of "substituted judgment." The important distinction in this dissertation research is the inclusion that a discussion of patient preferences in the decision-making process in many cases might be represented by a family via substituted judgment or may actually be the preference of the family and not the patient. The following section includes a review of the literature on the distinction between patient and family preference and their overlapping role in making treatment decisions for people with dementia.

2.2.2.2 Family preferences in medical decision making

For patients with dementia, the loss of cognitive function, decisional capacity, and physical function usually develop gradually, progressively, and somewhat predictably (Rabins, 2006). The cognitive and physical declines necessitate that family be involved in providing care and serve as surrogates in the medical decision-making process.

Two assumptions underlie surrogate decision making in the current model of biomedical ethics in the United States. Both assumptions are intended to honor the autonomy of the patient by basing real-time decisions on preferences expressed previously, thus using the ethical and legal standard of substituted judgment (Beauchamp, 2008). The first assumption is that patients have, or are able to generate, well-formed preferences about treatment in future hypothetical situations. Second, potential surrogates are assumed to be able to ascertain from patients what their goals for care and treatment preferences are.

The principle of substituted judgment assumes that surrogates understand patient preferences and correctly represent the wishes of the patient. Underlying accurate substituted

judgment, however, is the assumption either that patient preferences are stable over time or that surrogates understand the most recent and salient preferences of the patient. However, findings from the literature have shown that, when faced with hypothetical decisions about life-sustaining medical care, family members are not able to predict a patient's preferences at levels of accuracy beyond those expected by chance alone (Ditto, 2001; Sulmasy, 1999). Family surrogates consistently overestimate the frequency with which patients would want to receive treatment (Uhlmann, 1988). They also project their own preferences onto the patient. As such, the decisions that family members make often bear little resemblance to those that the patient would make (Ditto, 2001; Pruchno, 2008).

These findings are not much of a surprise. There is no clear-cut or deductive relationship between a person's overall values and beliefs and a particular set of medical choices. This is even more salient when the choices are subtle, the outcomes are uncertain, and the benefits are often delayed, as with chemoprophylaxis for CHD. With the rare exception of a patient and family who have had extensive and imaginative discussions of preferences for an array of treatments, knowing exactly what type medical treatment a person would chose given their current state is impossible. It is even more difficult when levels of treatments are introduced, such as less aggressive forms of treatment that have fewer risks but still have implications for quantity and quality of life.

The literature on surrogate decision making has contributed evidence and theories about factors that may influence treatment decisions of surrogates of older patients. They include the severity of the patient's cognitive status, perceived quality of life, and caregiver burden (Kayser-Jones, 1989; Uhlmann, 1991; Tomlinson, 1990). A study by Mezey (1996) found that spouses of dementia patients were more likely to forgo a particular treatment if the patient's cognitive

function was more severe (e.g., irreversible coma), the treatment was considered more burdensome (e.g., CPR), and their perception of the patient's quality of life was low. These findings were consistent for all of the life-sustaining treatments presented to spouses (resuscitation, breathing machine, feeding tube). Results for spousal beliefs on treatment were less consistent. Sixty-eight percent of spouses said that they would forgo antibiotics if their loved one was in a coma, but less than 10% said that they would forgo antibiotics if their loved one had a critical illness.

These results are relevant to our understanding of the effect of dementia on use of chemoprophylaxis for CHD. Unlike decisions about burdensome life-sustaining treatments that are often clear for families, treating or not treating CHD with medications is not so obvious to families. The outcome of continuing or foregoing chemoprophylaxis is unknown, and the treatment is lower burden. Yet, it is conceivable that if families are pressed to consider stopping or not starting chemoprevention, the same factors noted above—cognitive status, perceived quality of life and caregiver burden—would contribute to the decision-making process.

2.2.3 Physician value judgments

2.2.3.1 Physical vs. cognitive disability

Despite the promotion of autonomy, studies suggest that the values and beliefs of physicians may also play in a role the medical decision-making process. In one of the first studies of sociological elements on physician decision making, Crane found that in cases where seriously ill hospitalized patients had more cognitive disabilities physicians were less aggressive in treating the underlying disease as well as other complications (Crane, 1975). In a more recent study of Dutch physicians, the decision to not treat pneumonia nursing home patients with dementia with

antibiotics was influenced by the severity of the cognitive impairment. Patients with more severe dementia and less physical capacity for self-care, as measured by the Bedford Alzheimer's Nursing Severity scale, were less likely to receive antibiotics to cure pneumonia (van der Steen, 2002).

These studies demonstrate that the patient's cognitive level plays a role in the medical decision-making process, yet few have made claims as to the cause. Crane (1975) hypothesized that humans define "personhood" based on the ability to interact with others and participate in society. In the context of medical decision making, when patients lose cognitive capability and the traits that make them people, or what she describes as "social worth," they are less valued by physicians and not treated as aggressively.

Wolf-Klein and colleagues (2007) put forth a related medical-model explanation as to the variation in health care services for people with dementia. In an epidemiological review article, Wolf-Klein adopts the conceptual model that people with irreversible forms of dementia, no matter what their disease stage or level of cognitive or physical functioning, should be considered as having a terminal disease. This conceptualization justifies protocols for limiting the treatment of underlying conditions and focusing on palliative care and symptoms, hence following the similar pathways as those with terminal cancer (National Comprehensive Cancer Network and American Cancer Society, 2003).

2.2.3.2 Futility

The conceptualization of dementia as a terminal illness relates to the issue of futility and the question of "why treat" CHD if the patient is dying of dementia. For patients with dementia and CHD, observed variation in health services may very well be the outcome of futility judgments

being made by the physician. In one of the most cited articles on futility, Schneiderman and colleagues (1990) define futility in two forms: quantitative futility and qualitative futility.

Relative to the Eddy model, quantitative futility lies in the realm of gathering the evidence and is statistically based. For instance, if an intervention has shown to be ineffective in the past 100 cases, it would be regarded at futile. Qualitative futility is more subjective, yet there are few, if any, published studies of medical interventions that have failure rates of 100%. Most reasonably considered interventions do work at least occasionally. The question then becomes at what (lower) level of success can an intervention be said to be futile? And what other patient characteristics affect the determination of successful treatment? The answers to these questions are no longer objective measures of futility but rather subjective ones. Different physicians with different personal experiences, values, and definitions of "social worth" will define an "acceptable lower limit" and "success" differently.

An example of the variation in defining quantitative futility is a 1994 study by McCrary and colleagues. In this study 760 physicians were surveyed in three tertiary-care medical centers and asked to respond to the question, "Regarding terminally ill patients, I consider a treatment 'futile' if the likelihood of success is *X* percent or below." Thus, while 19% of the surveyed physicians would consider a treatment futile only if it had a zero percent chance of success, 23% would consider it futile if it had a better than 10% chance, and 5% of respondents would consider it futile even if it had an approximately 50-50 chance of success. Even if there were studies showing that an intervention had a success rate of zero percent, some physicians would still ask how similar the patients in the studies were to the patient under treatment, and if they were different in any potentially substantive way, the zero percent chance of success might not apply.

The concept of qualitative futility is even more subjective. As Truog (1998) has pointed out, it is not useful when making medical decisions to ask whether an intervention is futile. The question must be, "Futile in relation to what?" If the effectiveness of chemoprophylaxis for CHD for patients with dementia is judged by its success in preventing a future MI (a common clinical goal), physicians could consider the guideline recommended treatment effective. If, however, it is judged in relation to quality of life and the patient's experience at the end of life (a common patient goal), it may be ineffective given that the medication could increase the patient's length of time living with dementia and experiencing its effects.

2.2.3.3 Quality of Life

Many difficult choices in medical decision making include asking the involved parties to make an assessment of a patient's present or future quality of life. There is an expansive literature that attempts to define and measure quality of life as a construct or factor for making medical decisions (Walter, 1990; Thomasma, 1984; Pearlman, 1991). Research on quality of life in older patients, with and without dementia, has found that physicians frequently rate their patient's quality of life lower than their patients rate their own quality of life (Uhlmann, 1991). While many people believe that those with dementia live a life of negligible quality, findings show that people living with dementia who are able to communicate on some level have positive self-perceptions of their quality of life (Lawton, 1991, 1997; Rabins,1997; Rabins,1999; Ready, 2003).

The patient's quality of life at the time of medical decision making and predicated for the future are frequent considerations in medical decision making. Assessments of and judgments about the patient's quality of life, with or without a particular treatment, are often difficult to predict owing to uncertainties about the patient's diagnosis, response to treatment, disease

progression, and overall prognosis (Pearlman, 1983; Thibault, 1980). Other factors may also make quality of life difficult to accurately predict. These include physician's subjective values relative to the patient's characteristics, such as cognitive status (Crane, 1975), inadequate communication between the physician and patient (Anderson, 1999), and the physician's own fear of illness and death (Thomasma, 1984). These subjective values may impact the way physicians interpret and apply evidence about the risks and benefits of treatments and the way they present treatment recommendations to patients and families.

Pearlman and Jonsen (1985) conducted a study to better understand physician considerations of quality of life in medical decisions by presenting internal medicine and family physicians (n=205) with a patient management problem case study modeled after American Board of Internal Medicine certification examination questions. The case presented was a male patient with an acute exacerbation of chronic obstructive pulmonary disease. The patient was an elderly-looking 69-year-old who lived in a nursing home, was easily incapacitated by shortness of breath, and had recently had a 2-month hospitalization because of a similar respiratory episode. Other clinical data about respiratory performance were presented. The patient had no written documentation regarding preferences for treatment (i.e., advance directive) and had not expressed any information about treatment preferences to the physicians on this or previous hospital stays. Additional information about the patient was available but had to be requested by the physician study subjects.

The physicians performed several tasks during the study exercise, including (1) indication of treatment preference after the initial reading of the case, (2) indication of potential value of available (but unknown) case information, (3) selection of a limited amount of case information to acquire more detailed data about the case, (4) indication of a treatment decision as to whether

to use intubation or current therapy without intubation (after acquiring additional data), (5) explanation of the rationale for treatment decision, (6) prognostication regarding the patient's expected survival time. The results indicate that 37% of all physicians justified their decision about treatment, at least in part, by an explicit reference to the patient's quality of life. Of those physicians who decided to withhold mechanical ventilation, 49% stated quality of life as a rationale for their decision. Among the physicians who chose to intubate the patient, 29% cited quality of life as an influential factor. Additionally, physicians who considered the patient's survival time and social information were more likely to cite quality of life as a rationale for their treatment decision. The results from this study provide evidence that the consideration of quality of life in medical decision making is systematically observed and a common rationale for medical decisions to both treat and not treat a patient.

Evidence of the use of quality-of-life judgments in medical decision making in a hypothetical case was established by Pearlman, but actual assessment of quality of life in real-world decisions are complicated by the lack of good and consistent measures of quality of life. As a result, physician use of quality of life is often based on their subjective perception of the patient's quality of life. In a study of chronically ill elderly patients, Ulhmann and Pearlman (1991) investigated whether perceived quality of life by the physician is actually associated with patients' preferences for life-sustaining treatment. Participants included chronically ill, elderly outpatients (n =258) and their primary physicians (n=105). Patients and physicians were independently administered a questionnaire regarding patient quality of life and preferences for cardiopulmonary resuscitation and mechanical ventilation for the patient. Physicians rated patients' global quality of life, physical comfort, mobility, depression, anxiety, and family relationships significantly worse than did patients. Nearly all perceptions of the patients' quality

of life were significantly associated with the perceptions of their physician. Patient-physician agreement on patient global quality of life was not significantly associated with agreement regarding treatment preferences. From this study we can conclude that primary physicians generally consider their older outpatients' quality of life to be worse than what patients themselves state. Furthermore, physicians' estimations of patient quality of life are significantly associated with physicians' attitudes toward life-sustaining treatment for the patients. For the patients, however, perceived quality of life does not appear to be associated with their preferences for life-sustaining treatment.

The results from these two studies demonstrate that quality of life is a consideration of the physician in making treatment decisions, but that physicians' perception of quality of life may vary from and be lower than that of the patient and the family. These conclusions are important when considering the effect that dementia has on patients receiving chemoprophylaxis for CHD given the perception of low quality of life that many have about the experience of living with dementia. Section 2.3.3.2 discusses the implications of the patient's own judgment of quality of life on the use of health services as well the family's perception of the patient's quality of life.

2.3 PREDICTORS OF HEALTH SERVICES UTILIZATION

As discussed in the previous sections, the medical decision-making process by physicians for patients with dementia entails a variety of factors. The process includes combining the evidence of risks and benefits of treatment with subjective value judgments about the patient. While the Eddy framework considers each of these elements, we believe it excludes some important

patient-level factors that have been cited in the literature as possible predictors of health services utilization. The following section introduces the Andersen model, which is used in this dissertation research to understand and analyze the patient-level factors that may predict the use of chemoprophylaxis for patients with dementia.

The Andersen and Newman Behavioral Model of Health Service (Andersen & Newman, 1973) was first developed to predict and explain the use of formal personal health services (e.g., hospital services). It has since been refined and expanded (Andersen, 1995) and has been used to explain patterns of utilization for many types of health services, including medications (Sleath, 2004; Smith, 1999). This model, as shown in Figure 2.2, suggests that health care needs of the patient precipitate the use of health services and it assumes that a sequence of conditions surrounding the patient contribute to the type and volume of health services that a patient uses. The Andersen model also acknowledges the importance of external environments (e.g., the economic structure of health care or supply-driven variation) and individual patient characteristics that are categorized as predisposing, enabling, and care needs.

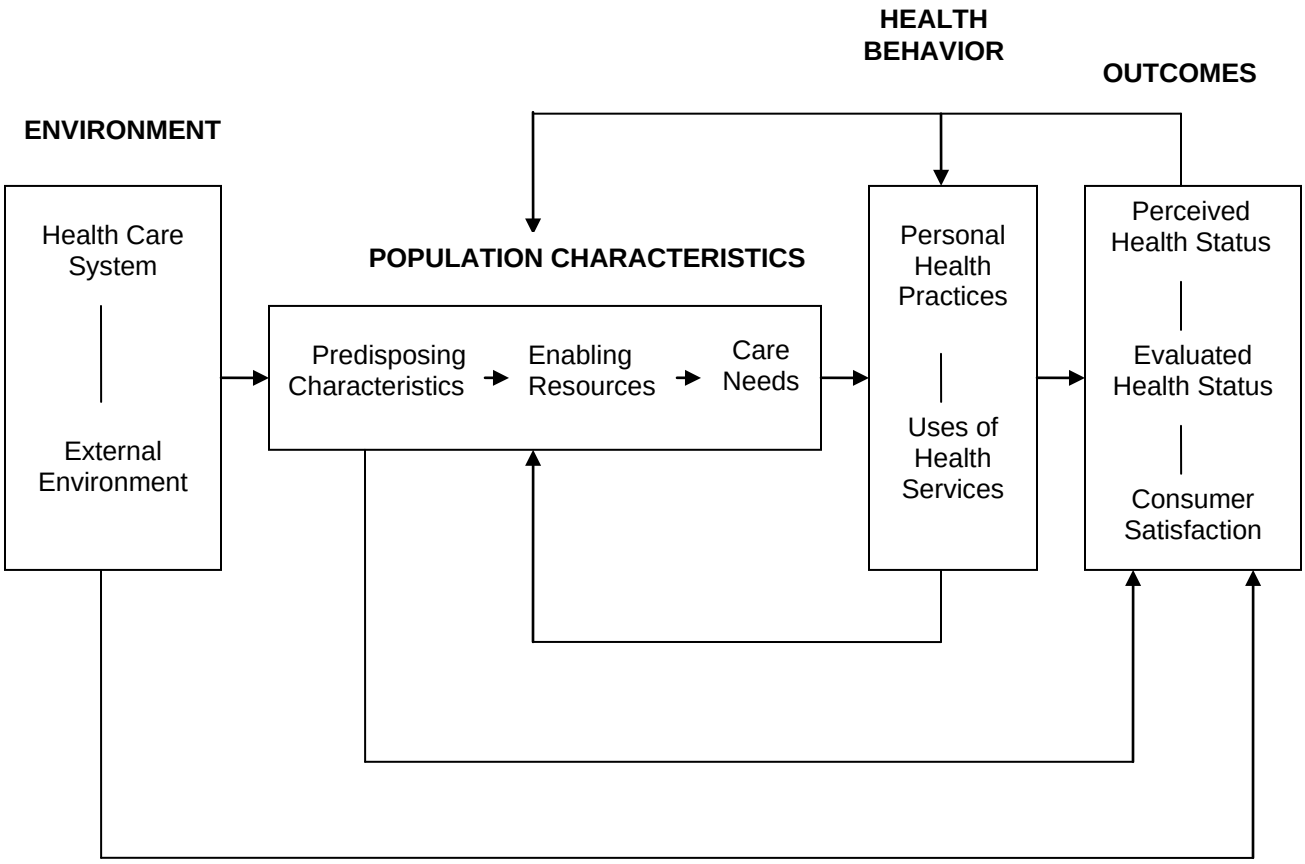


Figure 2.2: Andersen Behavioral Model of Health Services Use (1995).

2.3.1 Predisposing factors

In the Andersen model predisposing factors include exogenous variables such as patient demographics and variables that measure the social structure that directly affects an individual's need for a particular health service. These include age, sex, marital status, education, race/ethnicity, and occupation as well as a set of beliefs and attitudes toward health services and knowledge about health and disease. Because we believe that certain predisposing patient characteristics may have an impact on use of chemoprophylaxis for patients with dementia, section 2.2.1 uses the Andersen model to organize and summarize the findings from the literature regarding the predisposing factors that are included in the empirical analyses in this dissertation research.

A number of predisposing factors such as age, sex, and race have been shown to have an effect on the use of health services in general and on medications specifically (Lipton, 1988; Chrischilles, 1992; Fillenbaum, 1993). Each of these factors has its own vast literature regarding its predictive strength on the use of health services. The summary of the literature in the following sections focuses on the findings most salient to variation in health services for older adults in general, and, when available, specifically on variation in health services and medication for people with dementia. Many of the factors are correlated and difficult to "tease apart" and summarize individually, so applicable findings from the literature that present results for multiple factors will be reviewed jointly.

2.3.1.1 Age

Although age by itself is not a contraindication for most medical interventions, the ratio between treatment and benefit shrinks as people get older and experience comorbidity and frailty. Age is the strongest predictor and is the most significant risk factor for both the development of dementia and CHD.

Literature on the effect of age in predicting the use of health services spans the range of treatments from screening to life-sustaining treatments at the end of life. The impact of patient age, even in the absence of comorbidities, is important if it is shorter than the time period of achieving benefit from a particular screening (Sox, 1998). In this scenario, variation is appropriate and guidelines should explicitly exclude those who are not expected to live to realize the benefit from screening. An additional consideration for older patients is the reduction in benefit from screening that may be accompanied by an increase in burden.

Walter (2008) found that regular mammography rates among women ≥80 years old were associated with earlier stages of cancer, and of the 12,000 women who were diagnosed with cancer in the study sample, survival was not associated with mammography use. A summary of randomized trials on which current clinical practice guidelines for breast cancer screening are based (Coleman, 1992), demonstrate that the difference in breast cancer mortality between screened and unscreened women does not become noticeable until 5 years after screening, making it unlikely that older women with a life expectancy of less than 5 years will benefit from mammography.

A recent cross-sectional study of screening for colon cancer found that of 1,244 asymptomatic individuals in three age groups (50–54 years, 75–79 years, and ≥80 years) who underwent screening colonoscopy the prevalence of cancer was highest in the oldest group

(28.6%), yet the benefit achieved from the screening was only 15% of that achieved by the youngest group (.13 life years) due to shorter life expectancy, risk of immediate harm from the procedure, and time-until-benefit of the screening (on average 10 years) (Lin, 2006). Given the evidence on the benefits of screening, it is reasonable that age is a predictor of health services use.

In studies that look at the role of age in treating life-limiting illness, results consistently show that age affects the type of treatment and the overall rate. In a study of initial treatment patterns for lung cancer in Medicare beneficiaries, Smith and colleagues found that age had a direct effect on patterns of care for lung cancer and survival according to the type of therapy. Age was associated with lower likelihood of getting any treatment for lung cancer (OR=0.35, 95% CI=0.29–0.43) and among those who received treatment, older beneficiaries were less likely to receive more aggressive surgical therapy (OR=0.27, 95% CI=0.21–0.34) but more likely to receive less burdensome radiation treatment (OR=1.69, 95% CI=1.39–2.03) (Smith, 1995).

In research involving life-sustaining treatment, age has also been shown to be prominent negative predictor, especially in the presence of comorbid conditions (Vrakking, 2005). In a study of 271 cases from Dutch medical charts, Ubachs-Moust and colleagues (2008) found that age-related value judgments by physicians when deciding on treatment decisions were ubiquitous and present in all phases of the reasoning used by physicians to describe and justify the treatments they offered to patients. Setoguchi (2007) showed that among a cohort of 28,754 Medicare beneficiaries with at least one hospitalization for MI older beneficiaries were less likely to be prescribed a lipid-lowering medication, as were males and African Americans, after

controlling for other comorbidities. Krumholz (1998) demonstrated similar results for beta-blockers for adults ≥85 years of age.

Interestingly, age has not been found to be a positive predictor of patient adherence to chemoprophylaxis once the drug is prescribed. After controlling for comorbidities and number of prescribed medications, Sharkness and Snow (1992) and Coons (1994) found no relationship between age and rates of patient adherence.

2.3.1.2 Sex

Gender differences in the use of health services, such as cardiac revascularization procedures, have been noted, and it appears that they have persisted through time (Vaccarino, 2005). The literature on gender-based differences in the use chemoprophylaxis for CHD are mixed and reveal differences based on the class of medication. For example, McLaughlin (1996) conducted a study using the ACC/AHA guidelines as eligibility criteria for a study of 2,409 individuals hospitalized with MI. The results showed that of all eligible patients, women as well as patients over 74 years of age were less likely to receive antiplatelet medication (OR=0.7, 95% CI=0.6–0.9) and beta-blockers (OR=0.4, 95% CI=0.2–0.8).

Few studies look only at the effect of a single predisposing factor. In a study that looked at the effect of gender, race, and income, Rathmore and colleagues (2000) found that among 169,079 Medicare beneficiaries with CHD and at least one hospitalization for an MI, female patients were less likely to receive antiplatelet medication at admission (RR=0.98, 95% CI=0.97–0.99) and at discharge (RR=0.98, 95% CI=0.96–0.99). Subsequently, the same study showed that poorer patients and black patients were less likely to receive antiplatelet therapy and beta-blockers on admission and at discharge.

2.3.1.3 Race

Race has been studied as a predictor of health services both in terms of overall utilization of health services (Smedley, 2003) and regarding specific types of treatments, such as cardiovascular procedures (Whittle, 2003).

Variation among racial groups has also been cited for use of medications. Some studies have found that older American minorities are less likely than older whites to utilize prescription drugs or to increase their numbers of prescriptions over time (Briesacher, 2003).

Hanlon (1992) found, among an older community-dwelling cohort, that fewer African Americans reported the use of over-the-counter medications and total medications than did Caucasian Americans and that African Americans were less likely than Caucasian Americans to use cardiovascular drugs, as well as analgesic and central nervous system medications.

Among the studies that have looked specifically at chemoprophylaxis for CHD, Cooper (2002) showed in a national sample of patients hospitalized with acute myocardial infarction (AMI) that African American patients were less likely to be treated with lipid-lowering medication: 28.9% in comparison with 31.9% of non–African American patients (OR=0.87, 95% CI=0.83–0.91). Cooper also found in a multivariate analysis that female sex (OR=0.97, 95% CI=0.94–1.00), African American race (OR= 0.94, 95% CI=0.89–0.93), and older age (OR=0.82, 95% CI=0.78–0.86) are predictors of lower rates of lipid-lowering medications.

In contrast, Sanderson (2007) found no differences in the rates of aspirin, beta-blockers, or lipid-lowering medications, and higher rates of use of ACE inhibitors among African Americans. In a study across eighty-one acute care Veterans Administration hospitals, Peterson (2002) found that African American patients were equally likely to receive beta-blockers, more

likely than white patients to receive aspirin (86.8% vs. 82.0%; $P<0.05$), and marginally more likely to receive ACE inhibitors (55.7%).

2.3.1.4 Education

As a predictor of health services use, level of education is rarely studied as an independent factor. Findings from the literature reveal that to have a complete picture of which factors have an effect on variation in health care services utilization (e.g., race, ethnicity, sex, geographic region), the role of socioeconomic factors, such as education, income, employment, and insurance status, must be accounted for (Kaplan, 1993). In a study by Opotowsky and colleagues (2007) that looked at aspirin use for those with CHD, having a higher level of education was a significant predictor of aspirin use for men, but it had no effect for women. Studies that have investigated chemoprophylaxis use by race have found that even when level of education is controlled, non-whites have lower rates of use for aspirin (Rodondi, 2005), and among only women, African American women had lower rates of use for aspirin (OR=0.84, 95% CI=0.58–1.19; P=0.33) and lipid-lowering medications (OR=0.62, 95% CI=0.44–0.87; P=0.006) and slightly lower rates for beta-blockers (OR=0.83, 95% CI=0.61–1.16; P=0.30) but higher rates for ACE inhibitors (OR=1.32, 95% CI=0.92–1.90; P=0.12 [Jha, 2003]).

2.3.2 Enabling Factors

Enabling factors include the variables that describe a patient's ability to secure health services. These entail both community resources and personal resources such as personal finances, insurance status, informal or formal support for care, and socialization. These types of variables include both individual patient-level characteristics as well as health care system characteristics.

They are important in analyses of predictors and rates of utilization for health services, since some factors may have a direct relationship (e.g., number of nursing homes in a region and rate of utilization of nursing homes) or an indirect relationship (e.g., insurance status and site of care). The following section reviews the literature on enabling factors that we believe may predict use of chemoprophylaxis for patients with dementia.

2.3.2.1 Availability of health care providers and facilities and regional practice patterns

The differential supply of specialists and hospital capacity has been described in the literature as a cause of geographic variation in health care services across the U.S. (Wennberg, 1982). It is likely that differences in number of physicians, specialists, hospitals, and other types of care facilities could be an enabling factor that predicts health services utilization in different geographic regions. Research in quality of care for Medicare beneficiaries often uses variation as a proxy for the quality and efficiency of the care provided in a region. In the literature on variation, quality of health care is commonly measured by examining the care provided in a region that is low cost, highly effective, and of known medical benefit and is rarely contraindicated; in other words, evidence-based. The relevant literature for this research are findings that demonstrate that where Medicare beneficiaries live can impact the level and quality of health care services they receive in general (Baiker, 2005) and in terms of chemoprophylaxis for CHD more specifically (Krumholz,1998). Results from the National Cooperative Cardiovascular Project describe chemoprophylaxis utilization rates for Medicare beneficiaries with CHD across nine different geographic regions in the U.S. Among eligible beneficiaries who met the ACC/AHA criteria for use of beta-blockers, the overall rates varied from 43.6% in the Mountain region to 72.6% in New England (Krumholz, 1998).

2.3.2.2 Income

As noted above, measures such as income and education are often used as general measures of socioeconomic status, and at times in place of race, as a way to measure disparities in care. A study by Gornick and colleagues (1996) that looked at general rates of utilization among Medicare beneficiaries by income level found that less affluent non-minorities were more likely to be hospitalized for CHD episodes than more affluent non-minorities, but no differences were observed in the rates of cardiovascular procedures such as revascularization and angioplasty. In the same study, less affluent African Americans were less likely to be hospitalized for CHD episodes and to receive angioplasty and coronary artery bypass surgery. These findings about the effect of affluence on treatment patterns inform the research in this dissertation, since cognitive status is an individual characteristic that is being tested as a predictor of variation, and although all participants had Medicare as their primary insurance, other predictors must be considered and controlled.

2.3.2.3 Insurance status

The CHS study was conducted prior to the enactment of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Medicare Part D). As a result, the cost of chemoprophylaxis was borne either by the study participant or by their supplemental insurance, if they had a plan with drug coverage. Before Medicare Part D, data from the literature showed that the cost of drugs for Medicare beneficiaries was an important feature of under-utilization of prescribed cardiovascular medications, even among those with supplemental drug coverage (Federman, 2001). In a cross-sectional study of 1,908 Medicare beneficiaries with CHD, lipid-lowering medication ranged from 4.1% in patients with no supplemental drug coverage to 27.4% in patients with employer-sponsored drug coverage ($P<0.001$). The same study found less

variation for beta-blockers, but utilization was lowest for the group with no supplemental drug coverage to their Medicare insurance. Beneficiaries with Medicare and Medicaid had higher utilization of both drugs than those with only Medicare, yet lesser utilization than those with employer-sponsored drug coverage (Federman, 2001).

2.3.2.4 Living in a nursing home

In this dissertation research, the status of living in a nursing home is an important enabling variable for three reasons. The first is the prevalence of dementia among nursing home patients. It is estimated that between one-half and two-thirds of nursing home residents have dementia (Magaziner, 2000). Although CHS participants were not eligible for the study if they were in a nursing home at the time of enrollment into the study, 3% of the population were in a nursing home at some point during the study. It is possible that nursing home status may be a proxy for cognitive impairment or decline.

Second, data on patients in nursing homes show that are they are high users of prescription drugs. Two studies by the same investigator of twenty different U.S. nursing homes found that the average number of prescription drugs was 7.7 per patient (Beers, 1988; Beers, 1992). Higher rates may be an indicator of nursing home patients' multiple comorbidities as well as more advanced stages of illness. In a recent study of severely demented patients living in a nursing home, residents had an average of 14.6 medications prescribed in the 6 months prior to death. This same study found that as patients approached death, the types of medications change but not the overall number. Presence of cardiovascular disease among the study population was significantly associated with the total number of medications. Of those who were on a lipid-lowering medication 6 months before death (10%), utilization did not decline before death (Blass, 2008).

The third reason is related to the organizational structure in nursing homes. As compared to people in the community, multiple people have input into the medications that patients are prescribed and are involved in medication administration. Nurses, pharmacists, and social workers all contribute to the care planning process of nursing home patients and may influence physician prescribing. Additionally, if a nursing home patient is prescribed a medication, there is detailed documentation on when, where, by whom, and how the medication was administered. If a prescribed medication is not administered or is administered incorrectly, the facility (as per federal regulation) must document that episode as a medication error and must document how it happened and what steps were taken to correct and prevent it from happening again. This level of oversight is not routine for patients living in the community. A study of patients from the community entering a nursing home found that as many as 50% who had been prescribed medications were not taking them either at all or as prescribed (Sackett, 1979). We hypothesize that CHS participants with CHD who are in a nursing will be more likely to report taking chemoprophylaxis, despite their cognitive status, as a result of the oversight of medication administration in that setting.

2.3.3 Care need factors

Need factors include objective measures of a patient's health status as well as their self-perceived health status. Objective measures of a patient's health status, such as the presence of comorbid diseases, may be one of most useful and significant predictors of health outcomes (Walter, 2008). Yet the presence of comorbidities often produces complex situations in medical decision making, since the optimal care of one disease may be constrained or even contraindicated by another (Hoffman, 1996).

As predictive factors for receipt of chemoprophylaxis for CHD among patients with dementia, need factors include other comorbidities, the severity of their dementia as measured by things such as activities of daily living (ADLs), and functional status. Also included among need factors are clinical indicators that measure disease burden and have been found to positively predict disease severity and life expectancy. The following section summarizes the literature on the role of comorbidities, disease burden, and patient and family perception of health status on health services utilization. When available, specific data about people with dementia are reviewed.

2.3.3.1 Comorbidity

It has been well documented that rates of comorbidity among older people are higher than in younger populations and are associated with poor quality of life, multiple medications, high health care utilization, and mortality (Gijsen, 2001; Hoffman,1996; Field, 2004). Boyd (2005) estimates that 50% of all Medicare beneficiaries have at least two comorbid chronic diseases. Some evidence suggests that the degree of physician adherence to clinical practice guidelines may vary, depending on the presence of a comorbid condition. Frequently, the evidence to support decision making in a complex patient with multiple comorbidities may not be available, as complex patients are often excluded from the randomized controlled trials used in the development of guidelines. Carter and colleagues (2000) found that patients with CHD and diabetes were less likely to be taking ACE inhibitors, as compared with patients with CHD only.

Some of the most relevant research on the effect of comorbidity on utilization of heath services for older beneficiaries is in the area of primary prevention. In a study of female Medicare beneficiaries, those with a history of MI or diabetes or with limitations of ADLs and instrumental ADLs (iADLs) were less likely to receive a mammogram. Although this study did

not include any measures of cognitive status, limitations in ADLs and iADLs are common among those with both mild and moderate dementia (Ives, 1996).

A second study looking at primary prevention found that among eligible women 43 years or older, the likelihood of compliance with breast and cervical cancer screening decreased by 17% with every one unit of decline on the Charleson comorbidity index. Additionally, the rate of mammograms for women with stable angina was only two-fifths of that in women without angina (Kiefe, 1998).

With comorbidities come increased opportunities for burden of disease and symptoms. In a study of guideline adherence for diabetes, Piette and Kerr (2006) suggest that when comorbid conditions have a greater symptom burden than diabetes, the comorbid condition can dominate the medical decision-making process and have a negative impact on adherence to guideline-recommended care in diabetes. For patients with dementia, burdens of disease that may affect receipt of or adherence to guideline-recommended chemoprophylaxis begin at the earliest stages and persist. These include loss of procedural memory and inability to remember to take a medication; dysnomia, or inability to effectively communicate side effects due to medication; and dysphagia, or inability or refusal to swallow pills.

When dementia is the comorbidity with CHD, the treatment outcomes may be different than if the comorbidity is another disease that has only physical manifestations owing to value judgments about quality of life and social worth. For example, in a study that looked at adherence to guidelines regarding lipid-lowering medications, patients with dementia were more likely to have lower adherence over time, while the opposite was true for those with hypertension, stroke, CHF, or diabetes. Additionally this study found that patients who resided in a nursing home were significantly more likely to remain on their prescribed regimen (Benner,

2002). In another study, Heflin and colleagues (2002) investigated the effect of comorbid illnesses on the receipt of cancer screening for people over 65 years. The general findings from this study showed that the presence of comorbid conditions in older adults is not associated with a decreased rate of screening. Specific findings about the type of comorbidity were that when cognitive impairment is at least one of the comorbidities, lower rates of fecal occult blood tests (FOBTs) (OR=0.71, 95% CI=0.54–0.94) were reported as well as a trend toward lower rates of mammography.

2.3.3.2 Patient and family perceptions of health status and quality of life

The empirical work in this dissertation research tests the effect of dementia on the use of chemoprophylaxis and uses patient self-report as a proxy for physician-prescribed guideline-recommended therapy. Yet, research shows that when a patient is prescribed a medication and has the means to fill that prescription, he or she must perceive a need to adhere. Embedded in this perception are patients' knowledge, attitudes, beliefs, and expectations regarding disease progression with and without treatment (Byrne, 2005). Patients are more likely to adhere if they (1) perceive their illness to be serious, (2) expect the medication to help them or improve their quality of life (Andersen, 1995), or (3) feel as if they have some control over the disease (Leventhal, 1980). A study of adherence to cardiac rehabilitation showed that the more patients believe they have control over the symptoms and progression of their disease, the higher the levels of adherence (Cooper,1999). Applying these findings to patients with dementia and CHD, it is reasonable to think that patients may be less likely to adhere to chemoprophylaxis for CHD if they acknowledge their dementia as a progressive, terminal condition that they are unable to control. This acknowledgment may lessen their beliefs about the necessity of the medications,

given that preventing a subsequent MI in the short term may only extend their experience with and death from dementia in the long term.

Quality of life for patients with dementia is a well-studied area that has looked at numerous types of interventions to enhance a patients' ability to participate in and enjoy daily activities, including self-care and leisure, and improve opportunities for pleasure and interest (Albert, 1996; Lawton, 1997). The focus on patient quality of life for this dissertation research is to understand the role that patient quality of life has on the use chemoprophylaxis for CHD. No studies have looked at how a patient's quality of life, or their perceived quality of life by a family caregiver, influences the use of medications for CHD. The relevant literature on quality of life and adherence to treatment for patients with dementia reveals that if a patient (or caregiver) believes a treatment will improve quality of life, they are more likely to seek it out and adhere to it (Dooley, 2004).

Given the nature of dementia and the involvement of patients' families in caregiving and medical decision making, it is important to note that findings from the literature show positive correlations between the quality of life of patients with dementia and the quality of life of their family caregivers (Dunkin, 1998; Stuckey, 1996; Walker, 1998). This information is important, since when the patient's quality of life is difficult to assess, family caregivers are often used as proxy respondents (Berlowitz, 1995; Logsdon, 1995; Zimmerman, 1994). Applying these findings allows us to assume that if a family caregiver involved in medical decision making believed that a treatment would improve the patient's quality of life, the caregiver would be more likely to assist the patient in adhering to treatment. Two concerns with this theory are that family members, like physicians, have been found to underrate a patient's quality of life and the potential of improved quality of life from secondary chemoprophylaxis (with the exception of

nitrates for angina) is unknown. So, if a family member who is involved in medical decision making or in assisting their loved one with medication adherence, perceives the patient to have a low quality of life and is unsure about any benefits of the medicine to quality of life, lower utilization is likely. This may be amplified if the patient is unable to unwilling to take the medication and the burden on the caregiver to administer the chemoprophylaxis is greater.

2.4 UTILIZATION OF CHEMOPROPHYLAXIS FOR CHD AMONG PATIENTS WITH DEMENTIA

Elements of the Andersen and Eddy models provide some guidance in describing the effect of dementia on guideline-recommended chemoprophylaxis for CHD, yet neither model provides a comprehensive or complete framework. For people with dementia, the relevant medical factors as well as personal characteristics and value judgments by the physician, patient, and patient's family that complicate adherence to guidelines may also impact the use of chemoprophylaxis. The following section presents findings from specific studies that have investigated variation in use of health services for people with dementia both in general and for cardiovascular medication and treatments in particular. Section 2.4.2 includes a revised model that combines predictive factors from the Andersen and Eddy models as well as other potential predictors drawn from the literature and proposed in this dissertation research.

2.4.1 Variation in use of health services utilization for people with dementia

The association between cognitive impairment and use of health services has not been thoroughly investigated. Only a few studies have looked directly at the effect of cognitive impairment from dementia on the use of health services (surgical, medical, or pharmacotherapeutic). The following section is a comprehensive review of the studies that have investigated variation of health services among those with dementia and is organized based on the type of health service—cardiovascular or non-cardiovascular. When the results concern any type of treatment for CHD, those results are highlighted. Table 2.1 presents a summary of all studies.

2.4.1.1 Variation in cardiovascular health services

The most comprehensive study that has looked at differences in cardiovascular health services is a retrospective chart review by Sloan and colleagues (2004). This study used detailed clinical data from the Cooperative Cardiovascular project, combined with Medicare claims, to identify patients who were admitted to a nonfederal hospital between February 1994 and July 1995 with an MI. The sample included 123, 241 patients, of whom 5,851 (4.5%) had a history of dementia noted in their inpatient medical chart.

Descriptive findings of the sample reveal that, on average, patients with dementia tended to be older and were less likely to be white, less likely to be male, and much more likely to be admitted to the hospital from a nursing home (27% vs. 2%, $P<0.001$) and have a higher Charlson comorbidity index ($P<0.001$). For patients with dementia, higher mortality at 30 days and at 1 year post-hospitalization was observed.

Results from the analyses regarding treatment reveal differences in all outcomes, with the exception of aspirin and beta-blockers. The largest variation in treatment was observed for the more intense and aggressive treatment. Patients with a history of dementia were less likely to receive catheterization (RR=0.51, 95% CI=0.47–0.55), coronary angioplasty (RR=0.58, 95% CI=0.51–0.66), and cardiac bypass surgery (RR=0.41, 95% CI=0.33–0.50) than were patients without a history of dementia. Additionally, during hospitalization, patients with a history of dementia were less likely to receive thrombolytic therapy (RR=0.82, 95% CI=0.74–0.90).

For the less intense chemoprophylaxis, patients with a history of dementia were less likely to receive ACE inhibitors during their hospitalizations (RR=0.89, 95% CI=0.86–0.93) and at discharge (RR=0.90, 95% CI=0.86–0.95).

Applying these findings widely is limited because they include only those hospitalized with AMI, leaving out those who may have chosen less aggressive cardiovascular treatment and did not seek inpatient care. While the study does include measures of medication use at discharge, it does not account for subsequent treatment patterns for preventing future MIs. This may be particularly important in assessing the effect of dementia on setting goals of care for patients with CHD. Finally, a major limitation of the study is that dementia is identified via Medicare claims and does not include type, stage, duration, or severity of dementia. This method is likely to underestimate the number with dementia and overestimate the effect of dementia on use of health services utilization.

A second study that included cardiovascular health services as an outcome is a 1996 study by Hanlon and colleagues. In this study, medication use was compared in a cohort of 4,110 people ≥65 years living in five adjacent counties in North Carolina. Fifteen percent of the sample (n=564) had cognitive impairment as defined by the Short Portable Mental Status Questionnaire

(SPMSQ). Medication use was obtained by participant (or proxy) self-report and was compared by prescription vs. non-prescription, and then by class for all prescription medications. Cardiovascular medications were one class of medications assessed.

After controlling for age, sex, race, education status, functional status, comorbidities, and number of physician visits per year, the study showed that participants with cognitive impairment were 34% less likely to use any prescription medications. Unadjusted results reveal that participants with dementia report slightly greater use of cardiovascular medications (57% vs. 54%), although in the multivariable analyses, the results were not significantly different. Participants with dementia were more likely to report taking a lipid-lowering medication. Those with cognitive impairment were less likely to take analgesics (OR=0.66, 95% CI=0.52–0.83) but more likely to report taking central nervous system (CNS) drugs (OR=1.55, 95% CI=1.18–2.04). Within the CNS category, the largest variation was for antidepressants (7% vs. 3.2%, $P \leq 0.0001$). These findings are consistent with a study by Semla and colleagues (1993), who found that among a community with dementia, those with higher levels of cognitive impairment were more likely to use CNS medications.

The findings from the Hanlon study are limited for four reasons. First, and similarly to Sloan (2004), this study was cross-sectional and precludes any conclusions about causality and whether the dementia or mild cognitive impairment was the result of the differences in rates of utilization. Second, the categorization of cardiovascular drugs was broad and does not allow for any examination of differences among specific drugs, each of which has a different risks, benefits, and financial considerations. Third, dementia was assessed using only one measure and does not include stage or type of dementia to differentiate those with mild cognitive impairment from those with severe dementia. Fourth, the sample was representative of only one small region

in the southern U.S. As described in previous sections, regional differences in physician practice patterns may have an effect on overall utilization, making these findings difficult to apply broadly.

A third study conducted by Schmader, using the same dataset as the Hanlon (1996) study, looked at patterns of medication use among a community cohort with dementia (n=100), mild cognitive impairment (n=117), and intact cognition (n=303). A unique aspect of this study is the distinction between those with dementia and mild cognitive impairment using three levels of cut points on the Mini-Mental State Examination (MMSE). The participants were selected sample members of the Duke EPESE ("Established Populations for Epidemiologic Studies of the Elderly") who participated in face-to-face interviews in 1986–1987 for a separate study of incidence and prevalence of dementia in North Carolina.

Results reveal no significant differences among the three groups in the relative odds of using any prescription medications. However, the demented group took significantly fewer prescription medications than the mildly cognitively impaired group. Similar to the results found by Hanlon (1996), Schmader found that those with dementia were more likely to use CNS drugs and less likely to use analgesics (OR=0.54, 95% CI=0.39–0.75) than those without dementia and mild cognitive impairment. These similar findings may be due to patients with dementia under-reporting pain or to the undertreatment of pain due to the difficulty of assessing pain in patients with dementia (Frampton, 2003). Schmader's results differed from Hanlon's in that those with more sever impairment were significantly less likely to use cardiovascular drugs than those with only mild cognitive impairment (OR=0.70, 95% CI=0.49–0.99).

The limitations of this study are similar to those from the Hanlon study, given the use of the same dataset. An exception was the inclusion of a more sensitive measure of dementia due to

the creation of a category for those with mild cognitive impairment rather than combining these subjects with the dementia group or the cognitively intact group.

A study published in 2002 by Rodriguez and colleagues looked at the use of lipid-lowering medications among a community cohort of older Pennsylvanians with and without dementia. The study was based on a secondary data analysis from the longitudinal Monongahela Valley Independent Elders Survey (MoVIES). The sample for the Rodriguez study was drawn from participants who were still alive in wave 5 of the study (1996–1999). Dementia status was established during an in-home interview that included a battery of cognitive testing. Subjects identified in the interview as being demented or probable cases of dementia were referred for a clinical (diagnostic) evaluation. Use of lipid-lowering mediations was obtained by participant self-report and information gathered directly from the medication bottle during the in-home interview.

The sample included 845 subjects of which 170 (20.1%) were diagnosed with dementia. The dementia cohort was older (83.5 years vs. 79.6 years) and reported lower rates of use for lipid-lowering medications (3.5% vs. 10.8%, P=0.004). Multivariable analyses controlled for age, sex, education, self-reported heart attack or angina pectoris, stroke or TIA, hypertension, alcohol consumption, and smoking. Overall, participants with dementia were significantly less likely than those without dementia to report using a lipid-lowering medication (OR=0.39, 95% CI=0.16–0.95). Subanalyses that included only those with more severe dementia reveal no differences in the use of lipid-lowering medications.

Type of lipid-lowering medication, statin versus non-statin, was investigated to see if the patterns of overall use remained. Models that included only statins showed that those with

dementia were less likely to report using a statin, but the results were not statistically significant (OR=0.54, 95% CI=0.22–1.33, *P*=0.179).

The findings from Rodriguez support the general hypothesis that patients with dementia report lower rates of lipid-lowering medications. Some limitations of the study include sampling issues. Like the Hanlon and Schmader studies, this study included participants from only a single region in the U.S. Also, despite the longitudinal panel, analyses were essentially cross-sectional and did not account for changing dementia status or changing use of lipid-lowering medications over time. A final study limitation is that it did not control for relevant biomarkers, such as measures of serum cholesterol, that indicate clinically appropriate use of lipid-lowering medication. This is an important oversight, given the focus on utilization of only lipid-lowering medications.

Each of the studies summarized above included patients living in the community. Landi (1998) conducted a study to investigate the prevalence of comorbidities and treatment patterns among residents in nursing facilities. The retrospective cross-sectional study used data from the Health Care Financing Administration's (HCFA) Multi-state Case Mix Demonstration Project, which included nursing home resident data from facilities in five states (Kansas, Maine, Mississippi, New York, and South Dakota). The study variables included clinical information and functional status as well as other data from the Minimum Data Set (MDS) assessment for each resident in each faculty. Cognitive performance for residents was evaluated using the six-item Cognitive Performance Scale (Morris, 1994). In addition to the MDS data, the study included data about all medication use for the residents, organized by therapeutic class.

Of the 260,628 residents, 61% had some level of cognitive impairment, and not surprisingly, the more severe the cognitive impairment the more physical impairment and

assistance needed with ADLs. Overall, comorbid clinical conditions were more prevalent in the cognitively intact group than in the moderately or severely cognitively impaired group (3.0 vs. 2.8 vs. 2.4) ($P<0.001$). Regarding medications, Landi found that overall the average number medications per resident was significantly lower among those with moderate and severe cognitive impairment (6.2 ± 4.3 and 5.9 ± 4.6, respectively) as compared to residents with no cognitive impairment (7.3 ± 4.4). Results for medications by class reveal that residents with cognitive impairment are less likely to be taking medications in any class, with the exception of antipsychotics. For cardiovascular medications in particular, the group with the most severe cognitive impairment had the lowest rates of use compared to those with moderate impairment and no impairment (76% vs. 70% vs. 60%) despite similar rates of CHD (22% vs. 23% vs. 23%).

Results from the Landi study are in agreement with those found by Hanlon (1996) and Schmader (1998) in that demented patients were less likely to use cardiovascular medications and analgesics. However, opposite results were found for medications in the CNS class. Limitations of the Landi study include the inability to draw definite conclusions owing to the cross-sectional design. Additionally, the analyses did not control for duration of cognitive impairment or other comorbidities.

2.4.1.2 Variation in non-cardiovascular health services

The most recent study we reviewed that looks at variation of health services for patients with dementia was published in 2005 by Gorin . This study used the National Cancer Institute SEER registry to identify Medicare beneficiaries who were newly diagnosed with breast cancer stage I–III between January 1992 and December 1993. In this cohort, women who had at least two Medicare claims involving Alzheimer's disease (AD) before the diagnosis of cancer were

identified as having prevalent dementia. The sample included 50,460 breast cancer patients ≥65 years of age of whom 1,935 (3.8%) had dementia.

Descriptive findings from the study show that women with AD were more likely to be older, non-white, and have more comorbidities than those without AD (Deyo-Charlson index >3, 7.1% vs. 2.4%, $P<0.001$). Regarding the timing of diagnosis, women with AD were diagnosed with breast cancer at later stages, as measured by larger tumors and more likely involvement of lymph nodes.

Findings regarding treatment patterns reveal that patients with AD were 40% less likely to have surgery (OR=0.60, 95% CI=0.46–0.81). Additionally, patients with AD were less likely to receive radiation therapy (OR=0.31, 95% CI=0.23–0.41) and chemotherapy (3% vs. 11%; OR=0.44, 95% CI=0.34–0.58). The greatest variation occurred among those 80–89 years old. Analyses of all treatments show that the length of time with AD is related to the likelihood of receiving *any* treatment for breast cancer. The only instance in which AD patients did not receive lower rates of treatment compared to those without AD was for chemotherapy for those without metastases to the axillary nodes (Gorin, 2005).

The study's findings may be limited in general by biases in the SEER database, but also by the identification of dementia from Medicare claims data. Studies examining dementia diagnoses in medical claims have found that they have strong specificity but poor sensitivity (Wilcheksy, 2004). Additionally, the study lacked any data on the stage of dementia or the method of diagnosis (e.g., psychometric test or diagnostic imagining). Despite these limitations, they add to the literature of the likelihood for patients with dementia to experience lower utilization of health services.

Gupta and colleagues (2004) conducted a similar study to Gorin using the National Cancer Institute's SEER database to assess the prevalence and treatment patterns of colon cancer for patients with dementia. The cohort consisted of all patients ≥67 years of age in the SEER database diagnosed with stage I–IV colon cancer between January 1993 and December 1996 (n=17,507). Dementia among the cohort was 6.8% (n=1,184) and established by at least one Medicare claim with a dementia-related ICD-9 Clinical Modification Code.

Descriptive findings from the study show that those with dementia with were more likely to be older, female, reside in a lower income and/or urban neighborhood, and have more comorbidities.

Results from the multivariable analyses regarding diagnosis show that dementia patients were twice as likely to have colon cancer reported only after death (i.e., by autopsy or death certificate). Of those with cancer reported before death, patients with dementia were twice as likely to be diagnosed by use of noninvasive techniques rather than direct tissue biopsy (OR=2.02, 95% CI=1.77–2.55).

Findings about treatment variation reveal that living patients with dementia were 43% as likely to receive surgical resection (OR=0.43, 95% CI=0.33–0.70). Furthermore, among the patients with resected stage III colon cancer, dementia patients were only 20% as likely to receive adjuvant chemotherapy (OR=0.21, 95% CI=10.13–20.36).

Results from this study show that patients with dementia have distinct patterns of presentation, diagnosis, and treatment of colon cancer that differ from those without dementia. The limitations of this study are similar to Gorin in that claims data was used to identify dementia and the analyses lacked any information about severity of dementia, which may greatly affect diagnostic and treatment decisions.

Table 2.1: Summary of Literature on Dementia and Treatment of Non-dementia Diseases

Author, Year	Design	Sample	Utilization Measures	Results	Limitations
Gorin, 2005	Cross-sectional, retrospective cohort study, SEER database	N=50,460 Medicare beneficiaries with breast cancer; CON n=48,525 AD n=1,935 (3.8%)	Surgery (breast-conserving or mastectomy, if known), irradiation, and chemotherapy	Participants with AD had lower rates of any treatment (OR=0.55, 95% CI=0.42–0.74). The odds of AD patients having surgery were 40% less; irradiation, 31% less; and chemotherapy, 44% less than controls. The longer the amount of time with a diagnosis of AD the less likely the patient is to receive any treatment.	AD identified by Medicare claims. Analyses did not include stage or type of dementia. Method of AD diagnosis was unknown and not validated.
Gupta, 2004	Cross-sectional, retrospective cohort study, SEER database	N=17,507 Medicare beneficiaries with colon cancer; CON n=16,323 Dementia n=1,184 (6.8%)	Surgical resection and Adjuvant 5FU among those with stage III	Participants with dementia were 43% as likely to receive surgical resection (OR=0.43, 95% CI=0.33–0.70). Among patients with resected stage III colon cancer, those with dementia were only 20% as likely to receive adjuvant chemotherapy (OR=0.21, 95% CI=10.13–20.36).	Dementia identified by Medicare claims. Analyses did not include stage or type of dementia. Method of dementia diagnosis was unknown and not validated.

Table 2.1 (continued)

Author, Year	Design	Sample	Utilization Measures	Results	Limitations
Sloan, 2004	Cross-sectional, retrospective chart review, Cooperative Cardiovascular project	N=129,092 Medicare beneficiaries hospitalized for AMI; CON n=123,241 Dementia n=5,851 (4.5%)	Cardiac catheterization, coronary angioplasty, cardiac bypass surgery, thrombolytics, aspirin, β-b, and ACEi during hospitalization and at discharge	Patients with a history of dementia were less likely to receive catheterization (RR=0.51, 95% CI=0.47–0.55) coronary angioplasty (RR=0.58, 95% CI=0.51–0.66), cardiac bypass surgery (RR=0.41, 95% CI=0.33–0.50), thrombolytics (RR=0.82, 95% CI=0.74–0.90), and ACEi in hospital (RR=0.89, 95% CI=0.86–0.93) and at discharge (RR=0.90, 95% CI=0.86–0.95).	Only includes those hospitalized with an AMI, not subsequent treatment. Dementia was identified via Medicare claims data and does not include type, stage, duration, or severity of dementia.
Rodriguez, 2002	Cross-sectional analyses of 1 time-point from a longitudinal panel study, MoVIES database	N=845 participants who were alive in study wave 5 (1996-99); CON=675 Dementia n=107 (20.1%)	Number and type of LLM (statin vs. non-statin)	Participants with dementia had lower rates of use of any LLM (3.5% vs. 10.8%, *P*=0.004). In the adjusted model, participants with dementia were less likely to take LLM (OR=0.39, 95% CI=0.16–0.95). Of those with dementia all were taking a non-statin LLM. Severity did not impact use.	Did not differentiate between different types of dementia or disease severity or LLM use over time. Given the detail of type of LLM, the study did control for measures of serum cholesterol to assess for clinical appropriateness.

Table 2.1 (continued)

Author, Year	Design	Sample	Utilization Measures	Results	Limitations
Landi, 1998	Cross-sectional, retrospective cohort study, HCFA Multi-State Case-Mix Demonstration project	N=260,628 nursing home residents from five states during 1992-1995; CON=101,532 Moderate cognitive impairment n=106,054 Severe cognitive impairment n=53,042 (20.3%)	Medications by class and five different types of special treatment or care programs	Residents with cognitive impairment were less likely to receive cardiovascular medications, as well as respiratory medications, antidiabetic medications, narcotic analgesics, and NSAIDs, after control for prevalence of relevant comorbidities.	Included only a nursing home population, making it difficult to extrapolate management of community population with dementia.
Schmader, 1998	Cross-sectional, retrospective cohort study, Duke EPESE	N=4,110 people ≥65 years old living in five adjacent counties in North Carolina; CON n=303, mild cognitive impairment n=117 dementia n=100 (19.2%)	Prescription and non-prescription medications; nine different classes of prescription	Those with dementia were significantly less likely to use any prescription drugs (OR=0.65, 95% CI=0.45–0.93), cardiovascular drugs (OR=0.70, 95% CI=0.49–0.99), and analgesics (OR=0.54, 95% CI=0.39–0.75) compared to those with mild cognitive impairment.	Cross-sectional study of a single region in the U.S. Does not include timing of onset to make casual inferences about time-order relationships. Medication classes are broadly grouped without differentiation between individual medications.

Table 2.1 (continued)

Author, Year	Design	Sample	Utilization Measures	Results	Limitations
Hanlon, 1996	Cross-sectional, retrospective cohort study, Duke EPESE	N=4,110 people ≥65 years old living in five adjacent counties in North Carolina; CON n=3,546 Cognitively impaired n=564 (15.9%)	Prescription and non-prescription medications; 15 different classes of prescription	Participants with cognitive impairment were less likely to use any prescription medications (OR=0.66, 95% CI=0.48–0.90). Those with cognitive impairment were less likely to take analgesics (OR=0.66, 95% CI=0.52–0.83) but more likely to report taking CNS drugs (OR=1.55, 95% CI=1.18–2.04).	Cross-sectional study of a single region in the U.S. Does not include timing of onset to make casual inferences about time-order relationships. Dementia is assessed using only one measure and does not include stage or type.

Abbreviations: ACEi, ACE inhibitor; AD, Alzheimer's disease; AMI, acute myocardial infarction; β-b, beta-blocker; CNS, central nervous system; CON, control; EPESE, [Duke] Established Populations for Epidemiologic Studies of the Elderly; LLM, lipid-lowering medication; MoVIES, Monongahela Valley Independent Elders Survey; SEER, Surveillance, Epidemiology, and End Results cancer-based registry.

2.4.2 Revised model

The evidence-based decision-making model created by Eddy to describe the process of physician decision making and the patient-specific model created by Andersen to predict use of health services are helpful when considering the effect of dementia on variation in chemoprophylaxis for CHD. While the evidence from the literature supports the importance of each element contained in the two models, it is clear that describing them as two separate processes and parceling out the elements singularly is incomplete, given the confounding relationship of many of these factors are (e.g., age and comorbidity). For example, a study by Marwill (1996) that attempted to identify patient factors that influence physician recommendations for mammography reported that patient age alone does not predict fewer recommendations for mammography screening. When age was combined with cognitive impairment, it was a stronger predictor for not to screen with mammography for breast cancer ($P<0.001$). Similarly, physical functional status did not deter physicians from recommending screening with mammography, but when combined with residence in a nursing home it was a strong predictor against recommending mammography. This study emphasizes the importance of confounding patient factors that may, jointly, impact the use of chemoprophylaxis for patients with dementia.

Figure 2.3 presents an amalgamated model of the Eddy and Andersen models, and includes other important elements cited in the literature. The bolded elements represent those included in the empirical analyses of this dissertation research and are described in greater detail in Chapter 3. This model is used in this research to help conceptualize the range of factors that may predict use of evidence-based treatment for non-dementia illness for people with dementia.

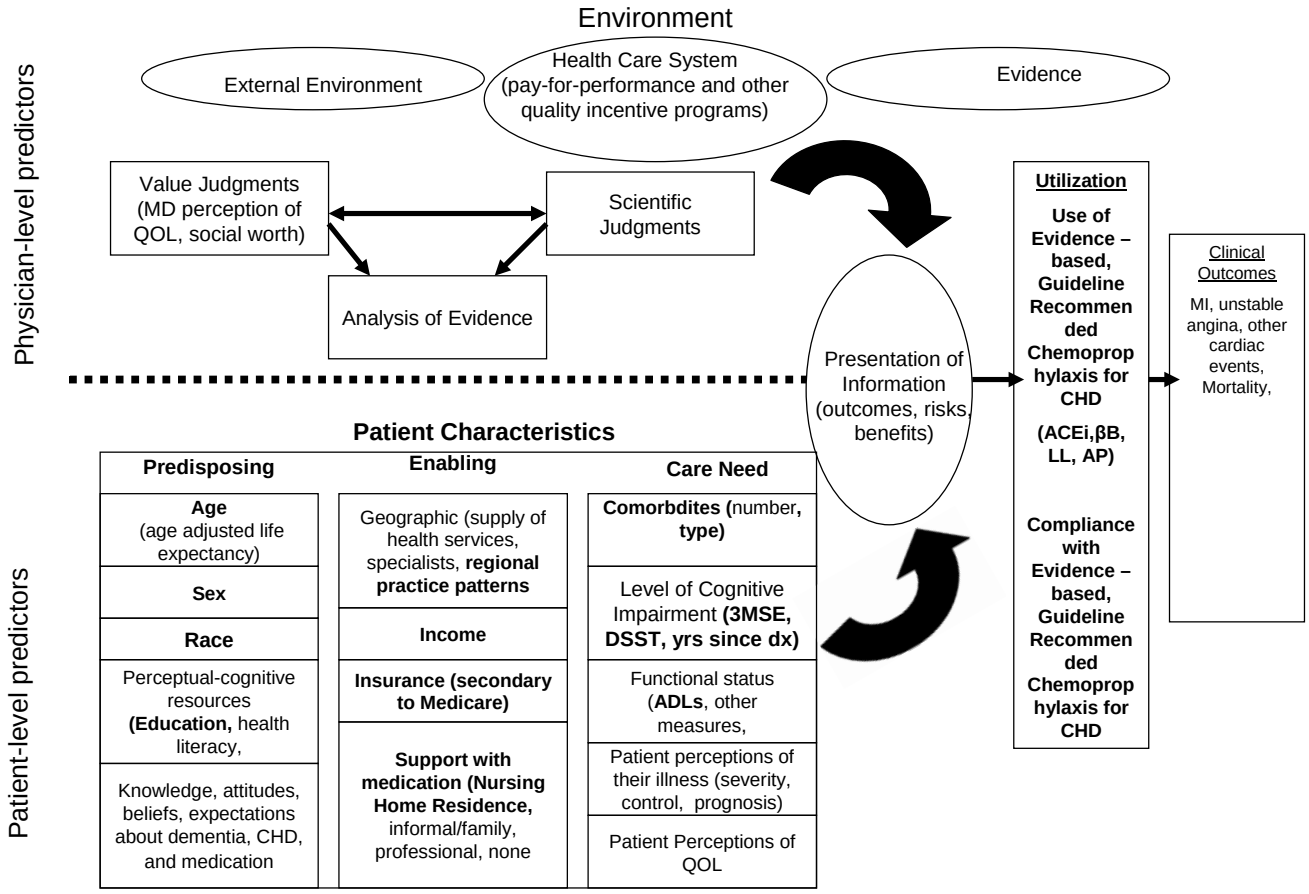


Figure 2.3: Conceptual Model for Predicting Use of Secondary Chemopreventive Treatments for CHD for Patients with Dementia.

3.0 DATA AND METHODOLOGY

This chapter outlines the dissertation's data and methodology. Section 3.1 describes the research design and data source. Section 3.2 defines the Cognition Study subsample of the Cardiovascular Health Study used in the analyses. Section 3.3 presents an overview of the analyses and research plan. Section 3.4 presents the strategy for preparing the data for analysis, and Section 3.5 describes the dependent and independent variables. Section 3.6 addresses issues of correlation and measurement reliability and validity. Section 3.7 discusses multivariate model specifications. Section 3.8 details the study's multivariate analytic methods. Finally, Section 3.9 describes the sensitivity analyses that were performed and presented in Appendix C, F, G, and H.

3.1 RESEARCH DESIGN AND DATA DESCRIPTION

This dissertation analyzes data from the Cardiovascular Health Study (hereinafter called CHS), a population-based, longitudinal study of risk factors for the development and progression of coronary heart disease and stroke in adults over the age of 65 years.[1] Initially funded by the

[1] This dissertation uses a secondary data analysis as the method of research. Secondary data analysis is the utilization and analysis of existing data or information that was collected for the purposes of a prior study, in order to pursue a research interest which is distinct from that of the original work. Sources of secondary data analysis often include official records collected by government agencies and previously collected measures from private or federally funded research projects (Cnossen, 1997).

National Heart Lung and Blood Institute (NHLBI) in 1988, it was renewed for a six-year period for data collection in 1994 with all analyses scheduled completed by 2009.

The National Institutes of Health describe the CHS as the most extensive study undertaken by the NHLBI to study cardiovascular disease exclusively in an older population. It originated from the recommendations of a 1986 NHLBI workshop on the management of coronary heart disease in the elderly.

The CHS study recruited 5,888 men and women from four US communities (Forsyth County, North Carolina/Wake Forest University; Sacramento County, California/University of CA-Davis; Washington County, Maryland/Johns Hopkins University; and Pittsburgh, Pennsylvania/University of Pittsburgh) who participated in extensive clinic examinations for evaluation of markers of subclinical cardiovascular disease. The original CHS cohort totaled 5,201 subjects. A supplemental cohort of 687 subjects, who were predominately African-American, was recruited in year five of the study (1992). The population from the Pittsburgh Field Center was entirely urban while the other three sites recruited a mixture from urban and rural populations.

Eligible subjects were sampled from Medicare eligibility lists in each of the four field center sites. Those eligible included all persons living in the household sampled from the Health Care Financing Administration (HCFA, now known as the Centers for Medicare and Medicaid Services, CMS) sampling frame, who were 65 years or older at the time of examination, were not living in an institution (such as a nursing home or assisted living), were expected to remain in the area for the next three years, and were able to give informed consent and did not require a proxy respondent for any questionnaires at baseline. Potentially eligible individuals who were

wheelchair-bound in the home at baseline or were receiving hospice care, radiation therapy or chemotherapy for cancer at baseline were excluded.

All subjects were examined annually from 1989 through 1999 with the exception of the supplemental cohort, who were examined from 1992 to 1999. A major emphasis of the CHS study is its focus on subclinical cardiovascular disease. Subclinical disease is an illness that stays below the surface of clinical detection with no recognizable clinical findings. The most extensive evaluations were at study entry and again in 1992-1993 to assess change in subclinical disease measures. From 1999-2009 the cohort was followed with bi-annual phone calls to assess study endpoints, including: myocardial infarction (MI), stroke, congestive heart failure, peripheral claudication (pain in the legs when walking, due to insufficient oxygen delivered to muscles), angina, transient ischemic attack (TIA) and death.

Additional data collected at the annual clinic examinations were measures of cognitive function using the Modified Mini-Mental Status Examination (3MSE) and the Digit Symbol Substitution Test (DSST). The 3MSE is a measure that uses an index of global cognitive performance with scores ranging from 0 to 100 (Teng, 1987). It is widely used in clinical settings to screen for dementia. The 3MSE provides a summary score that evaluates various dimensions of cognition (memory, calculation, orientation in space and time, language, and word recognition). The DSST explores attention and psychomotor speed. Subjects are given a code table displaying the correspondence between pairs of digits (from 1 to 9) and symbols, and they have to fill in blank squares with the symbol that is paired to the digit displayed above the square. The subjects have to fill in as many squares as possible in 90 seconds. The range of scores is from 0 to 90 (Wechsler, 1981). For subjects in the CHS who died or were unable to complete a 3MSE at their annual visit, a proxy measure of cognition was collected using the Information

Questionnaire for Cognitive Decline in the Elderly (IQ CODE) (Jorm, 1989). The IQ CODE lists 26 everyday situations where a person has to use their memory or intelligence. Examples include: “Remembering where to find things which have been put in a different place from usual” and “Handling money for shopping”. Each situation is rated by the proxy for amount of change over the previous year, using a five point scale of: much improved, a bit improved, no change, a bit worse, and much worse (Jorm, 1989).

Other relevant data collected by CHS includes functional status, measured by activities of daily living (ADLs), pharmaceutical drug use, and information on clinical outcomes, such as MI, dementia, and death. The CHS included adjudication committees for all events that were suspected as cardiovascular events, the development of dementia, and deaths. CHD adjudication committees provided disease specific “end point” information in the study. Information from participant’s next of kin regarding the circumstances and history of any illness was also collected.

Data from the CHS are available to investigators who have a demonstrated research interest and who identify a CHS sponsor. To obtain data for this dissertation, approval from the University of Pittsburgh’s Institutional Review Board was obtained (University of Pittsburgh IRB #0408086) and an ancillary CHS study proposal was submitted to and approved by the CHS Coordinating Center. Appendix A includes the IRB approval for this dissertation research.

3.2 SUBSAMPLE DEFINITION

The sub-population of interest for this research includes data from the Cardiovascular Health Study Cognition Study (CHS-CS). CHS-CS is an ancillary study to CHS that tested a series of specific hypotheses related to the incidence and determinants of dementia.

The CHS-CS subsample includes 3,602 participants from the CHS study who had both a cerebral magnetic resonance imaging (MRI) and Modified Mini-Mental Status Examination (3MSE) as part of the annual CHS data collection from 1991-1994.

Identification of dementia within the sample was made by a standardized protocol that was developed in 1998-1999 (study year 11) for the CHS-CS ancillary study. All eligible participants (n=3602) were divided into categories of high or low risk for developing dementia based on cognitive testing from previous years, changes in 3MSE and DSST scores, nursing home admissions, being dead or alive, and history of stroke. Table 3.1 describes the criteria used to determine high risk for dementia.

Due to sample size restrictions in three of the study site centers (Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland) only the whites classified as high risk for dementia were subjected to detailed neuropsychological and neurological testing for the diagnosis of dementia, but all of the participants belonging to a minority group were subjected to detailed neuropsychological and neurological testing for the diagnosis of dementia. At the Pittsburgh site (n=927) all participants were subjected to a detailed evaluation regardless of classification of high or low risk. Those labeled as low risk had no further follow-up other than routine CHS data collection. Following the neuropsychological and neurological testing at each of the sites, cases of dementia were reviewed by the dementia adjudication committee who reviewed all data and made a final determination of cognitive status.

Table 3.1: Criteria for defining high risk of dementia within CHS-CS cohort

Subject Alive 1998-1999	Subject Dead 1998-1999
At least 1 of the following criteria must be met to be classified as high risk	
3MSE[a] score <80 during at least 1 of last 2 clinic examinations.	3MSE[a] score <80 during within 2 years of death.
> 5 point decline in 3MSE from time of MRI to last contact	> 5 point decline in 3MSE from time of MRI to the year closest to death
TICS[b] score of <28 *and* IQ CODE[c] score >3.6	TICS[b] score of <28 *or an* IQ CODE[c] score >3.6 within 2 years of death, Diagnosis of dementia in at least 1 medical record (inpatient or outpatient, admission or discharge), a history of incident strike during the CHS study, belonging to a minority.
Had an incident stroke	
Diagnosis of dementia in at least 1 medical record (inpatient or outpatient, admission or discharge)	
Residing in a Nursing Home	

Abbreviations: 3MSE, The Modified Mini-Mental State Examination.
[a] The 3MSE has been found to be an efficient screen to determine persons at high risk of dementia (Lopez, 2003).
[b]The Telephone Interview for Cognitive Status (TICS) is an 11-item screening test that was developed for the assessment of cognitive function in patients with dementia who are unwilling or unable to be examined in person (Brandt, 1988).
[c]Informant Questionnaire for Cognitive Decline in the Elderly (IQ CODE) is a questionnaire that can be filled out by a proxy of an older person to determine whether that person has declined in cognitive functioning. The IQ CODE is often used as a screening test for dementia (Jorm, 1989).

Following dementia status adjudication, the distribution of the sample consisted of 707 subjects with dementia, 2318 without dementia, and 577 with mild cognitive impairment, but not classified as having dementia (n=3602). For the analyses in this dissertation, participants identified as having dementia at entry into the study (1989 or 1992) are labeled as having dementia at baseline and those who have a date of onset for dementia at any year after their baseline are and labeled having dementia starting in the year of onset. To be consistent with other published studies using CHS-CS data, participants identified with mild cognitive impairment but who never develop dementia during the study period are considered not demented (Lopez, 2003).

Of the 3602 participants in the CHS-CS, 1087 had CHD at baseline or developed CHD sometime during the study making them eligible for guideline-recommended chemoprophylaxis for CHD. Given that the main outcomes of interest for this research are use of four sub-classes

of chemoprophylaxis for CHD, only those participants who develop CHD are included the analyses. Figure 3.2 presents the sampling for this research.

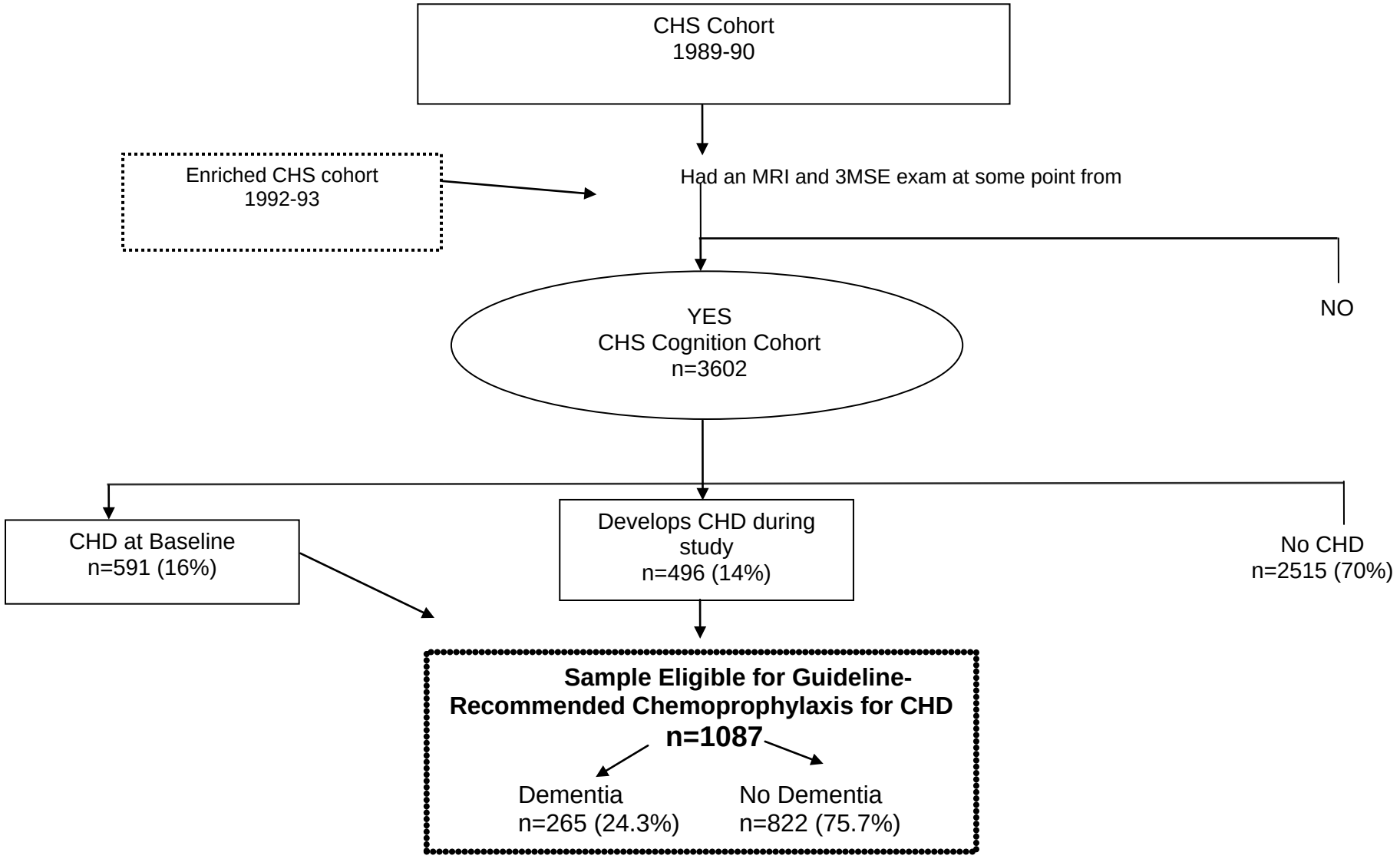


Figure 3.1: Analytical sample of participants with Coronary Heart Disease in the CHS-CS cohort

The CHS-CS study data are unique compared to other secondary datasets that include cognitive status information because they provide clinically adjudicated dates of disease onset for both dementia and CHD. In previous research that investigated the effect of dementia on treatment for CHD (Sloan, 2004; Hanlon, 1996, Schmader, 1998) the inclusion of dementia as a main variable of interest was limited to people with a diagnosis of dementia in a medical chart or identified in secondary administrative databases, such as Medicare claims data, or based on cognitive test scores only. A major strength of the CHS-CS data used in the analyses for this dissertation is that it provides a rich sample of subjects where both the CHD and the dementia diagnoses are defined by a standardized research protocol, and a committee of experienced clinicians who reviewed all data.

Despite the strength of the CHS-CS data, it is important to note from a study design perspective, that there are still many difficulties in establishing the true date of onset for dementia, particularly retrospectively. By definition, the onset of dementia is insidious and progression is gradual (McKahnn, 1984). Dating the onset based on the criteria used in this study (and certainly based on primary care physicians' identification) likely underestimates the duration of illness for most patients, because the majority of people with dementia have symptoms for several years before receiving a diagnosis (Boustani, 2003; Corrada, 1995).

Having a date of onset for both CHD and dementia across all ten years of the CHS-CS allows for time series analyses to explore whether the timing of disease onset has an impact on use of chemoprophylaxis for CHD. For those who develop dementia first, we predict that they will be less likely to initiate chemoprophylaxis. Of the subjects who develop CHD first, we predict that the rate of chemoprophylaxis for CHD will decease following the onset of dementia. These predications are based on theories from the medical ethics literature that differentiate

between acts of commission and omission regarding the discontinuation of medical treatment. While there is no moral difference between not starting medical treatment versus stopping medical treatments that people are receiving, data show that patients, families and physicians are often more willing to make a passive decision to not initiate a treatment than they are to make an active decision to stop a treatment (Brock, 1994). In the case of participants with dementia, we predict that not starting chemoprophylaxis for CHD is more prevalent than stopping chemoprophylaxis for CHD once it has been initiated.

3.3 ANALYSIS OVERVIEW

Three interrelated research questions concerning the use of chemoprophylaxis for CHD direct the empirical analyses for this dissertation. The dependent variables for all three questions are four sub-classes of cardiovascular medications recommended by the American College of Cardiology/American Heart Association (Ryan, 1996) for people with CHD (incidence of a myocardial infarction (MI) or unstable angina). They include Angiotensin- Converting Enzyme (ACE) Inhibitors, beta-adrenergic blocking agents (Beta-blockers), HMG-CoA Reductase Inhibitors (lipid-lowering medications), and anti-platelet medications such as Cyclooxygenase inhibitors (Aspirin) and Adenosine diphosphate (ADP) receptor inhibitors (such as Plavix®). Two additional outcome variables were created to measure compliance with these medications. For those participants who had CHD, if they reported taking two, three or all four of the medications they were labeled as 50-100% compliant and those with CHD who reported taking none of the four medications were labeled 0% compliant.

The main independent variable for all three analyses is dementia status. Given the different focus in each research question, dementia status and the interaction variables between dementia status and age was measured differently in each analysis. Independent variables were selected for the multivariable analyses based on their theoretical relevance, their statistical properties (significance and confounding) and by using the Eddy framework for medical decision making (Eddy, 1990) and the Andersen Behavioral Model of Health Services Use (Andersen, 1995) as guides.

Descriptive, bivariate, and multivariable analytic techniques were used in this research. Analyses for three empirical research questions generally proceeded in the following stages: (1) inspection of the data, (2) descriptive analyses, (3) bivariate and confounding analyses, (4) multivariable analyses, and (5) post estimation parameter tests and model predictions. To investigate the relationships among dementia and use of chemoprophylaxis, we first examined bivariate associations between all predisposing, enabling and care need covariates and each sub-class of chemoprophylaxis and the two compliance measures (0% and 50%-100%) and calculated unadjusted odds ratios (OR) for each pair. To better understand the specific role of certain covariates as confounders for the association between dementia status and use of chemoprophylaxis, we examined the unadjusted odds ratio of chemoprophylaxis for each covariate, the change in the odds ratios after adjusting for dementia status, and the fully adjusted odds ratios controlling for the remaining covariates that demonstrated a significant association with use of chemoprophylaxis (p value $\leq$<0.10) in bivariate analysis and covariates that were forced into the model based on theoretical significance. All analyses were performed using Stata/SE, version 10 (Statacorp 2006). Table 3.2 presents the dissertations research questions, hypotheses, rationale and associated analytical approach.

Table 3.2: Research questions, hypotheses, rationale and analytic strategy

Research Question	Hypotheses	Rationale	Analytic Strategy
Q1: Are Medicare beneficiaries with dementia *and* CHD[a] less likely to report use of evidence-based chemoprophylaxis for CHD compared to those with CHD but without dementia*?*	Medicare beneficiaries who have dementia *and* CHD will have lower rates of chemoprophylaxis for CHD than their non-demented peers.	When physicians make treatment decisions they will be less likely to follow evidence-based guidelines for people who have dementia because (1) CHD guidelines do not address how to treat patients with a limited life expectancy due to dementia; (2) value judgments about decreased quality and lessened social worth will make treating co-morbidities a lower priority and make them less likely to offer treatment.	Longitudinal panel analysis of subjects with CHD. The model uses 10 years of data and compares dementia status with use of chemoprophylaxis. Weighted GEE[b] models for ACEi[c], βB[d], LL[e], and AP[f] drugs and 0% and 50-100% compliance. Assessment of the significance of the beta standardized coefficients and odds ratios with supplementary graphical presentations.
Q2: Are Medicare beneficiaries who develop *dementia first* then develop CHD less likely to report using evidence-based chemoprophylaxis for CHD compared to those who develop *CHD first* then develop dementia?	Medicare beneficiaries who develop dementia before CHD are less likely to take secondary preventive medications because (1) it is easier to not start a medication than to stop one that has already been started and (2) their dementia will be more severe at the time of CHD onset.	The ordering of the disease development matters in medical decision -making given that physicians and families find it harder to stop a treatment for a preexisting disease than they do initiating a new treatment for a new disease, especially for low burden, low risk treatments like chemoprophylaxis.	Longitudinal panel analysis of subjects with CHD that includes the timing of disease onset. The model uses 10 years of data and compares the time of dementia onset with use of chemoprophylaxis. Weighted GEE models for ACEi, βB, LL, and AP drugs and 0% and 50-100% compliance that adjust for timing of dementia onset, presence of dementia at baseline, and within subject correlation.
Q3: Are Medicare beneficiaries who develop CHD *first* more likely to discontinue evidence-based chemoprophylaxis for CHD after they develop dementia?	The rate of chemoprophylaxis will be higher for Medicare beneficiaries who develop CHD before dementia, but discontinuation of evidence-based chemoprophylaxis will occur as their number of years with dementia increases and cognitive function declines.	It is easier for physician to not start a treatment (a passive act of omission) for someone with a life-limiting illness such as dementia than it is to stop a treatment (active act of commission) given that the later requires explicit conversions about the patient's terminal status and futility of chemoprophylaxis.	Longitudinal panel analysis of only subjects who develop CHD before dementia. The model uses 10 years of data and compares discontinuation of chemoprophylaxis among subjects who develop CHD before dementia using the number of years with dementia as the independent variable. Weighted GEE models for ACEi, βB, LL, and AP drugs. Assessment of the significance of the beta standardized coefficients and odds ratios with supplementary graphical presentations.

Abbreviations: CHD, Coronary Heart Disease; GEE, Generalized estimating equations; ACEi, Angiotensin- Converting Enzyme Inhibitors (ACE inhibitors); βB, Beta-blockers; LL, HMG0CoA Reductase Inhibitors (lipid-lowering drugs); AP, aspirin and other anti-platelet drugs.

3.4 DATA PREPARATION

This section describes the steps used to prepare the CHS data prior to analysis. Primarily this involved reviewing the data that was available from the CHS, preparing a proposal and data request form and submitting it to the CHS Coordinating Center, inspecting the structure of the data as well as the collection tools and instruments used to collect the data. All of the primary independent variables were created from the original CHS database while some existing variables were recoded, such as race, education, insurance status and income. For example, date of dementia onset was provided in the original CHS file, and the binary dementia status variable measuring dementia each year (yes or no) was crated from the date of onset variable.

Preparing the data involved becoming familiar with the technical language of the study, studying the details of the CHS and CHS-CS sampling, reviewing all data and the corresponding codebook, and reviewing the levels of measurement for each potential variable. All original data were provided by the CHS Coordinating Center in a "wide file", meaning that each record, or row in the dataset contained all years of data of the information about an observation. For example, questions 1 and 2 in Table 3.3 were asked of every participant in each year in the study. In the original wide file, there was one row per study participant and that question was coded MIY2, NEWMIY3, NEWMIY4……,NEWMIY11.

After review of all potential variables, relevant variables for the analyses were identified and converted to a "long file." Converting the wide data file to a long file created a single row for each observation for each year in the study so there is one observation per unit for each time period in the study.

Table 3.3: Sample questions from the CHS annual medical history form

Selected Medical History Questions	Selected Medication Use Questions
MIY2 Has a Dr. ever told you that you had a MI or myocardial infarction? **NEWMIY3-11** Since we saw you last year, has your doctor told you that you have had an MI or myocardial infarction? **ANGY2** Has a doctor ever told you that you had angina? **NEWANGY3-11** Since we saw you last year, has your doctor told you that you have had angina?	**ASPRY2-11** Have you taken aspirin in the last 2 weeks? **DAYASPY2-11** If yes, on how many days?

CHS provided a codebook with the dataset and most survey instruments used to collect the data were accessible online. None of the variables used in the analyses were affected by skip patterns in the instruments, but given the number of years data was collected and the advanced age of the cohort, missing data were examined to ensure that it was random or due to death or drop out of the study. No deaths occurred prior to study year 5 (1992) and by study year 11 (1999) 21% of the sample was dead.

3.5 MEASURES

As described in Chapter 2, conceptual models for evidence-based medical decision-making (Eddy, 1990) and to predict the use of health services among individuals (Andersen, 1995) were used in this research. Elements of these models guided the organization of the literature review and the selection of variables for the analyses.

3.5.1 Dependent variables

The Eddy model of medical decision-making consists of two main steps. The first step involves the processes of gathering and analyzing available evidence about the possible outcomes that are associated with different treatments. The four guideline-recommended medications and measures of compliance of these medications that are the dependent variables in this research represent the best available evidence for the medical management for the secondary prevention of CHD (Ryan, 1996).

3.5.1.1 Guideline-recommended chemoprophylaxis for CHD

The dependent variables include self-reported use of ACE inhibitors, beta-blockers, lipid-lowering medications, antiplatelet medications. While each drug has their own contraindications, none are contraindicated based on the cognitive status of the patients. Table 3.4 presents descriptive statistics for study years 5-11 for all participants in the CHS-CS with CHD and their use of chemoprophylaxis. All years can be found in Appendix B.

Table 3.4: Unadjusted use of chemoprophylaxis among participants with CHD, No. (%)

Dependent Variable	Study Year 5	Study Year 6	Study Year 7	Study Year 8	Study Year 9	Study Year 10	Study Year 11
ACE inhibitors	110 (15)	120 (16)	138 (18)	151 (20)	151 (21)	175 (24)	181 (24)
Beta-blockers	185 (26)	197 (26)	207 (27)	203 (27)	213 (29)	239 (32)	256 (35)
Lipid-lowering medications	84 (12)	107 (14)	113 (15)	125 (17)	146 (20)	181 (24)	206 (28)
Anti-platelet medications	445 (62)	457 (62)	475 (63)	455 (62)	419 (59)	443 (62)	445 (65)

Abbreviations: CHS-CS, Cardiovascular Health Study-Cognition Sample; ACE Inhibitors, Angiotensin-Converting Enzyme Inhibitors

For purposes of the analyses, all dependent variables were dichotomized and expressed as taking the drug (1) or not taking the drug (0) in each study year or as compliance (0% yes or no or 50-100% yes or no). The CHS medication data is based on participant self-report. CHS data did not include prescriptions (unless part of the hospital record) or outpatient medical records that may have included prescription information. These methods of measurement raise two study limitations. The first is that use of chemoprophylaxis is based on participant self-report not what was actually prescribed to them by a physician. Studies have reported that older patients adherence to prescription medications may range from only 26% to 59% (Cooper, 1982; Col, 1990). Given this, the data used in this study may underrepresent rates at which physician prescribe guideline -recommended chemoprophylaxis for CHD.

Second, any medication reported by the participant would have been prescribed by a physician in the community, and we were unable to assess or control for the community physician's knowledge about the patient's cognitive status. There is likely a disconnect between the community physician's awareness of the patient's cognitive status vs. the documentation of dementia in the CHS study given their focus on dementia and detailed diagnostic procedures. For

patients with mild dementia, cognitive status may have little to no effect on physician prescribing.

3.5.1.2 Compliance with chemoprophylaxis for CHD

Two additional dependent variables were created to measure compliance with the four sub-classes of medications. These variables were calculated by summing the total number of medications reported for each year for all participants with CHD and divided by the total number of non-missing medications for that year. For example, a subject would be labeled as 100% compliant for a study year if they had CHD in that year and reported taking all four medications in that year. The compliance variable was then organized as either 0% compliant (i.e. report taking none of the four medications) or 50-100% compliant (i.e. report taking at least two, three or all four medications).

3.5.2 Independent variables

3.5.2.1 Main independent variables

Dementia status is the main independent variable for the three empirical analyses. The analyses for the three research questions include different measures of dementia that address three different, but connected concepts: binary and categorical measures of dementia status each year based on date of onset and cognitive status and decline based on a widely used and validated measure over time observed throughout the study. Table 3.5 presents the primary independent variables selected for each aim and the alternative specifications that were tested in sensitivity analyses for each aim.

Table 3.5: Primary and secondary measures of independent variable by study aim

Dementia Status Measures	Study aim 1	Study aim 2	Study aim 3
Dementia (present in that year)[a]	✓		
Dementia at baseline [b]	†		
Prevalent Dementia [c]	†		
3MSE Score Less than 80[d]	†		†
DSST Score Less than 30[e]	†		†
Dementia before CHD [f]		✓	
Disease status each year [g]		†	
No disease (suppressed category)			
CHD only			
Dementia only			
Both diseases			
Number of years since dementia diagnosis [h]		†	✓

✓ Signifies primary independent variable selected for study aim and † signifies alternative specification tested for each study aim.
Abbreviations:3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test; CHD, Coronary Heart Disease.
[a] Dementia status each year (yes or no) based on adjudicated CHS date of onset (e.g. labeled as having dementia from year of onset until death).
[b] Upon entry into the CHS-CS cohort (e.g. dementia baseline year 1989 or 1992).
[c] Prevalent dementia (e.g. the CHS-CS retrospective classification based on date of initial study evaluation).
[d] 3MSE score of less than 80. The Modified Mini-Mental State Examination (3MSE) is a 100 point questionnaire test used to screen for cognitive impairment. The 3MSE samples a range of cognitive abilities from short-term and delayed recall to temporal and spatial orientation. It is used in clinical settings to screen for dementia and to estimate the severity of cognitive impairment at a point in time and to follow the course of cognitive changes in an individual over time (Teng, 1987). A score of < 80 was selected as a cut point to measure dementia and change in cognitive status based on previous research methods used in the CHS-CS (Kuller, 1998; Lopez, 2003).
[e] DSST score of less than 30. The DSST is a measure of attention and speed. In previous CHS-CS studies the Spearman correlation between the DSST and the 3MSE at study year 5 was .55. A low digit symbol score was classified as <30 and was selected as a cut point to measure dementia and change in cognitive status based on previous research methods used in the CHS-CS (Kuller, 1998; Salthouse, 1978)
[f] Sequence of dementia onset in relation to date of CHD onset (e.g. a binary static measure of developing dementia before CHD, yes or no)
[g] Disease status each year for CHD and dementia (e.g. a categorical measure that captures a participant's disease state in each year)
[h] The number of years since the CHS-CS date of onset. Year of onset labeled as 1.

3.5.2.2 Control variables

Selection of additional control variables was guided using the Andersen Behavioral Model of Health Services Use (Andersen, 1995). This conceptual model framework consists of three central constructs: predisposing, enabling, and need-for-care or factors that predict the use of health services.

Predisposing variables are characteristics of the patient that contribute to the propensity to use health services. These include demographic characteristics, social structure variables, and attitudes and beliefs about health. The predisposing variables included in this research include: age, sex, race, and level of education.

Consistent with the majority of published research using CHS data, the race variable was coded as white (1) and non-white (0). Different of functional forms (age^2, age^3, etc.) of the age variable were reviewed, as well as the continuous age variable and creating different cut points for age (See section 3.7.1 for more details). For the analyses, the age variable was centered on the mean age of the sample for each year. Centering on the mean subtracts the mean value from all of the age data points and shifts the scale of a variable to adjust for multicolinearity. The education status variable was dichotomized as high school or less (1) or more than high school (0). Some research has noted that level of education is an important variable to include when investigating the effect of cognitive impairment since it has been documented that higher rates of dementia have been found among people who have lower levels of education. It has been noted that these findings may be a result of their lower cognitive status throughout life and poor performance on cognitive status measures such as the 3MSE and DSST (Fitzpatrick, 2004).

As defined by the Andersen model, enabling variables are conditions that permit an individual to use health services. In most health services research, insurance status or other

"access to care" measures are included as enabling variables. The four enabling variables used in this research include supplementary insurance, income, CHS study site, and residence in a nursing home.

Access to care is not a major predictor for this research since all participants (as defined by CHS recruitment eligibly) had Medicare as their primary health insurance for both inpatient and outpatient medical care. Additionally, the data was collected before the enactment of Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Medicare Part D), so there was no uniform insurance that was available for Medicare beneficiaries that covered prescription medications. Nonetheless, some participants may possess supplementary insurance coverage that they purchased, have as part of a retirement package, or qualify for based on income (Medicaid) that could include some coverage of prescription drugs. Two different measures of supplemental insurance were tested in the models: (1) a categorical variable that measures type of supplemental insurance in each year that the data was collected (study years 6-7 and study years 9-11) and (2) a dichotomous variable that measures if a participant ever had a form of supplemental insurance (private, Medicaid, other) or was ever without supplemental insurance. Selection of which insurance variable to include in the multivariable model was based on results of the bivariate analyses and the effect of missing data on the model since the insurance information was only collected in five of the ten study years.

Income was included as an enabling variable despite the fact that the effect as a predictor was minimized due to the low cost of the medications examined in this research. We believe it is important to test in the full model since other research has demonstrated income as a predictor of medication compliance in the elderly (Balkrithnan, 1998), especially prior to Medicare Part D. Income was coded as a "1" if a participants annual income was $24,999 or below and "0" if

$25,000 or higher. These cut points were based on data from the Census Bureau's annual Current Population Survey (CPS) that showed the mean household income for Medicare beneficiaries in 1996 (CHS study year 8) was $29, 280 although the median was significantly lower at $19,448 (US Census Bureau, 2009).

CHS was a national multi-center study with four locations. Study site was included in the models to control for variation in sampling and to serve as a proxy for geographic variation of prescribing patterns since the four sites represent different regions of the US (Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pennsylvania) and studies have found geographic variation in use of chemoprophylaxis for CHD (Krumholtz, 1998).

The final enabling variable included in the multivariable models measures residence in a nursing home. Living in a nursing home, in each year, was coded as a binary variable "1" for yes and "0" for no. This variable is important for two reasons. First, residence in a nursing home is correlated with severity of dementia. Second, participants in a nursing home have their medications managed by the nursing home staff. This management includes getting the medication prescribed, getting the medication paid for (source varies), and administering the medication to the resident. It is likely that any disconnect (as a result of the study design limitations) between what is prescribed and what a participant reports taking is eliminated for those participants in a nursing home.

Care need variables are arguably the most important predictors of use of health services for patients with dementia and include both the patient's perception of their illness and quality of life as well as objective measures of functional and cognitive status. The CHS data did not include patient self reported quality of life or their beliefs about their illness. Care need or illness

level variables that were available and included in the multivariable models are dementia status (measured differently for each study aim), activities of daily living, hypertension, diabetes, and kidney disease.

Activities of daily living (ADLs) refer to the basic tasks of everyday life, such as eating, bathing, dressing, toileting, and ambulating. In the CHS data, ADLs are measured on a scale from 0 (no assistance with ADLs) to 6 (severe physical disability and requires full assistance with ADLs).

There are a number of health conditions, some of which are comorbid with CHD, that could increase the likelihood of a person using chemoprophylaxis for CHD. Each model controlled for these clinical factors including: history of hypertension, diabetes, or kidney disease, or cancer. For the antiplatelet and compliance models, any form of arthritis was also included since aspirin (one of the antiplatelt medications) is a common medication used to treat the symptoms of arthritis.

3.5.2.3 Interaction variables

It is well documented that the likelihood of dementia increases with age (Mitchell, 2009). Given this correlation, an interaction variable of age and dementia status was tested for inclusion in each model to assess if the causal effect of age on chemoprophylaxis differs by dementia status.

3.6 RELIABILITY AND VALIDITY OF THE MEASURES

In general it is difficult for researchers conducting secondary data analyses to perform reliability and validly checks on data. Of the two measurement properties, the evidence for validity is

generally weaker and more controversial for secondary data (Carmines, 1979). The CHS data were collected in a variety of methods over a ten year time period. Built into the CHS were mechanisms to ensure reliability and validity of the data. As described above, the dependent variables in this research, use of chemoprophylaxis for CHD, was collected based on report from the subjects. At the annual visits, subjects would bring with them all of their prescriptions and the information was recorded by the CHS staff. Data collected regarding medications included drug type, name, and dose.

Measurement error and the associated problems of reliability and validity are concerns of researchers using secondary data (Carmines, 1979). While few studies have addressed measurement issues regarding prescription drug use and older persons with dementia, the general consensus in the literature is that self-report health data from community dwelling older adults is an acceptably reliable and valid method of measuring prescription drug use (Lubeck, 2005).

The data for the independent variables used in this dissertation were collected using a combination of methods. Some variables, such as the predisposing variables sex, race, date of birth, and highest level of education achieved were self-reported survey data collected at entry into the study, while other clinical variables, such as hypertension, diabetes and renal insufficiency were asked each year and documented based on participant self-report and then adjudicated by the CHS through confirmation from treating physicians or from hospital discharge summaries.

The measures for dementia status were created using CHS-CS dates of onset and classifications that have been published by Lopez (2003) and described in Section 3.2. An important feature of the CHS-CS coded data regarding dementia is that the study used MRI neuroimagining and scores from cognitive performance instruments (3MSE, DSST, IQ CODE)

administered from 1991-1994 to determine the date of onset. Participants coded as having prevalent dementia, the actual onset of dementia could have been anytime from before the study started to up and including 1994, the final year of assessments to determine prevalence. Using this measure of dementia status does not allow the accurate incorporation of time of onset into the model so it was not used as a primary impendent variable, but was tested in the sensitivity analysis for aim 1.

The CHD variable was created using two clinical indicator variables of CHD, myocardial infarction (MI) and angina pectoris. In each year of the study, participants were asked is they had a (new) MI or angina. If they answered positively for either question at the baseline interview the study, they were determined to have prevalent or existing CHD. If they answered yes to either question in subsequent years, they were considered to have developed CHD in that study year. CHD status was coded as a binary yes (1) and no (0) variable with the year of development initiating the change. For example, if a participant did not have angina or an MI in study years 2-4, but developed angina in study year 5, the CHD variable for that participant would be coded as 0,0,0,1,1,1,1,1,1,1 in study years 2-11.

3.7 MULTIVARIABLE MODELING

3.7.1 Model specification and functional form

The greatest assets of longitudinal data are the stories that can be told about how a population changes over time and the possibility to distinguish key types of causality between the variables. Until fairly recently, researchers using longitudinal data have been limited in their strategies for

creating a model for analysis given the lack of random distribution of longitudinal data. Researchers were often forced to transform the dependent variable or use other methods of aggregating the dependent variable to approximate normality prior to analysis.

Creating the most appropriate model using longitudinal data and variables that are correlated within subjects can be a challenge. Failing to take into account correlated longitudinal data can lead to incorrect estimations of the model parameters. For example, in the CHS-CS data, participants' positive use of beta-blockers in study year 2 is highly correlated with their positive use in year 3 given that this particular medication taken for a chronic condition that persists over time.

Successful model building is part science, part statistical method, part experience and theoretical knowledge about the problem. Variables were selected based on the frameworks by Eddy and Andersen and based on their hypothesized impact of receipt of chemoprophylaxis for CHD. The goal is to provide a complete set of variables that can explain confounding effects in the dataset since some variables alone may not be significant, but taken collectively and combined with other variables, confounding could be present.

This approach initially yielded 8 potential ways to measure the independent variable (dementia status) and 19 potential control variables in the constructs described above (predisposing, enabling, and care need). The distribution and potential outliers of each variable were reviewed. Given the nature of the longitudinal data, none were excluded based on distribution alone.

The age variable was considered an especially important predictor in this research given the epidemiology of dementia and the possible effect that age could have on the ongoing use of chemoprophylaxis. The functional form for age was tested using $age^{2,}$ age^{3}, age cut into 10

groups and three groups (≤75, 76 -85, and ≥86), the proportion of the categorized age variable, and the age variable centered at the mean of the sample. Based on univariate analyses and to adjust for multicolinearity the age centered on the mean was selected as the primary measure of age for all models.

The level of education variable, while not highly correlated with the dependent variables, did not appear to be confounding or a strong predictor based on the bivariate analysis. The decision was made to keep that predisposing variable in the full multivariable models given the results from other CHS studies that showed level of education as a positive predictor of dementia (Fitzpatrick, 2004).

3.7.2 Choosing a link function and distribution

The analyses in this dissertation use a binomial distribution and logit link function given that all outcome variables have a binary response (i.e. taking an ACE inhibitor "yes or no"). Using this link function allows for the regression equation to make the interval from 0 to 1 and is expressed as $g(x)=\log[\mu/(1-\mu)]$ (McCullagh, 1989).

3.7.3 Choosing a correlation structure

The generalized estimating equation (GEE) approach is becoming more popular in longitudinal studies. One reason it is cited as an optimal method is that a GEE models allow the use of a working correlation structure that may not be correct, yet the regression coefficients are still consistent and asymptotically normal (Pan, 2002). However with time-varying covariates, like

those in the CHS data, it is the working correlation matrix that allows GEEs to estimate the best models that account for the correlation of responses (Liang 1986). Using the wrong correlation structure is inefficient (Fitzmaurice, 1995), may violate an important assumptions in GEE, or produce biased estimates (Pan, 2002). Specification of the most accurate form of correlation of response within participants is an important process for the GEE model building.

The variables in these analyses are correlated within participants' over time. Given this, an autoregressive correlation structure was selected since it is specified to set the within-subject correlation as an exponential function of the lag period. In an effort to retain as many of the correlations groups as possible, a lag period of 1 year was selected. The theory behind this choice is the assumption that if a person is on a particular sub-class of chemoprophylaxis in t_1, the likelihood of that person being on the same medication in t_1+1 is correlated.

3.8 MULTIVARIABLE ANALYTIC METHODS

3.8.1 Generalized Estimating Equations

This dissertation uses longitudinal panel data with repeated measures that are correlated within a participant over time. To avoid making incorrect conclusions about the data and incorrect inferences about the regression coefficients, each analysis takes into account correlation within repeated observations on the same participant. Fitzmaurice (1995) demonstrated that when faced with an independent variable that varies within a cluster (i.e. a time-dependent covariate in a longitudinal study), the efficiency of estimators declines with increasing correlation.

Additionally Fitzmaurice found that the errors are particularly large for cases in which the correlation within subject is highly positive or highly negative.

Efficiency in the estimators was a major concern when preparing the data for analysis for this dissertation. It was determined that a repeated measures ANOVA approach to the problem was inadequate because it does not use a model of the covariates among related observations to increase the efficiency of the parameter estimates, which normally requires a balanced and complete data set that has normally distributed response variables.

The generalized estimating equation (GEE) approach was selected based on the correlated, repeated measures of participants and the binary dependent variables. GEEs were developed by Liang and Zeger (1986) and Zeger and Liang (1986) as a means of testing hypotheses regarding the influences of factors on binary and other exponentially distributed response variables correlated within participants across time. A GEE analysis produces marginal or "population averaged" estimates of effect . Estimates from this model are the log odds ratios of the population averaged effects of treatment. GEEs model the average value of the outcome variable for each subset of participants who share the same value of the predictor variable. They are an extension of Generalized Linear Models (GLM), which facilitates regression analyses on dependent variables that are not normally distributed (McCulloch, 2001; Nelder, 1972). GEE also allows the researcher to specify a within-person correlation structure to account for within-person correlations in the outcome variable over time. For every one-unit increase in the covariate across the population, the GEE model provides results of how much the average response would change (Zeger, 1988; Zorn, 2001).

3.8.2 Analytic strategy

Descriptive and univariate analyses were conducted for each dependent variable. Descriptive and bivariate analyses were conducted for each independent, control, and interaction variable within the three constructs (predisposing, enabling and care need). To better understand the specific role of certain covariates as confounders for the association between dementia status and use of chemoprophylaxis, we examined the unadjusted odds ratio of chemoprophylaxis for each covariate, the change in the odds ratios after adjusting for dementia status, and the fully adjusted odds ratios controlling for the remaining covariates that demonstrated a significant association with use of chemoprophylaxis (p value $\leq$<0.10) in bivariate analysis and covariates that were forced into the model based on theoretical significance.

Cut points for binary variables were reviewed and the continuous variables were reviewed to ensure the correct scale. Next, the models were reviewed for possible relevant interactions (e.g. dementia and age). Only the independent and interaction variables differ in the full multivariate models for each research aim. All dependent and control variables are the same for each full multivariable model across each aim.

The initial inspection of the data revealed that because of two waves of CHS recruiting (1989 and 1992), subjects in each cohort were not equally contributing to the population averaged results. Sampling weights were created for each subject for each year based on the probability of each subject being missing for both cohorts. Sampling weights are needed to correct for imperfections in the sample that might lead to bias and inaccurate parameter estimates and to compensate for unequal probabilities of selection.

3.9 SENSITIVITY ANALYSES

Two types of sensitivity analyses was co were conducted. The first compares the results from the final models that used the auto regressive correlation structure with those using an exchangeable correlation structure. The results for the final models using the exchangeable correlation structure are reported in Appendix C. As expected, we did not find any difference between the results from the two types of correlation structures.

The second sensitivity analyses include comparing the result for the full and final models with alternative measures of dementia status for each study aim. Appendices F, G and H present the results for the full and final models.

4.0 RESULTS

The empirical research conducted for this dissertation specifically tests the hypothesis that the rates of use of evidence-based chemoprophylaxis for CHD is different in patients with dementia compared to those who do not have dementia. The methodology employed is a secondary data analysis of a longitudinal dataset that was originally collected as part of the Cardiovascular Health Study (CHS) to study risk factors for the development and progression of CHD. Detailed information on cognitive status was also collected in CHS and adjudicated and analyzed as part of the ancillary Cardiovascular Health Study-Cognition Study (CHS-CS). Chapter 4 presents the results of the research and is organized according to the three study aims as outlined in Table 3.2. Section 4.1 presents general descriptive data. Sections 4.2 and 4.3 present the results of the bivariate and multivariate analyses, respectively. Each section is organized by study aim and then by the results for each dependent variable (self-reported use of ACE inhibitors, beta-blockers, lipid-lowering medications, antiplatelet medications, and compliance with medications).

4.1 DESCRIPTIVE STATISTICS

Descriptive statistics were calculated on all study variables. A total of 1087 participants in the CHS-CS cohort developed CHD during the study period, making them eligible for guideline-

recommended secondary chemoprophylaxis for CHD. Of those, 973 (89.5%) were enrolled as the first cohort in 1989-90 and the additional 114 (10.5%), predominately African American participants, were enrolled as a second cohort in 1992-93. This dissertation uses ten years of data and adjusts for the delayed entry of the second cohort with sampling weights. Section 4.1.1 presents the descriptive statistics of the sample.

4.1.1 Independent variables

At the baseline year, the mean age of the sample is 72.9 years (SD=5.05). In study year 5 (baseline year for the second cohort) the mean age is 75.6 years (SD=5.21). By the end of the study (1999) 21.2% of the sample died. Gender is evenly split between male (52.5 %) and female (47.8%). Race is predominantly white (928 white; 157 black; 2 other). The mean level of education was 13. 9 years (SD=4.6) with 57% of sample achieving a high school or higher levels of education. Income levels ranged from 5% reporting under $5,000 per year to 13% reporting $50,000 or more in annual income. Sixty-three percent of the sample reported an annual income level of $24,999 or below. Information of supplemental insurance to Medicare is variable for study years 6, 7, 9, 10, and 11 only. In study year 6, 69% have private supplemental insurance, 5% Medicaid, 13% report some other form of supplemental health insurance, and 7% report no insurance to supplement their Medicare coverage. Descriptive statistics, by dementia status, for study year 2 (1989), year 5 (1992; the first year of the second cohort), and year 11 (1999) are presented in Table 4.1.

Table 4.1: Sociodemographics by dementia status by year

	1989 (N=973)		1992 (N=1087)		1999 (N=862)	
Variable n (%)	**Participants without Dementia (n=948)**	**Participants with Dementia (n=25)**	**Participants without Dementia (n=1005)**	**Participants with Dementia (n=82)**	**Participants without Dementia (n=672)**	**Participants with Dementia (n=190)**
Age, y,						
≤75	680 (72)	7 (28)	562 (55)	25 (30)	76 (11)	7 (4)
76-85	257 (27)	12 (48)	408 (41)	44 (54)	447 (67)	89 (47)
86-95	11 (0.1)	6 (24)	26 (3)	12 (14)	92 (14)	59 (31)
≥96	0	0	9 (1)	1 (2)	56 (8)	35 (18)
Sex						
Male	517 (55)	18 (72)	517 (51)	50 (61)	335 (50)	89 (47)
Female	431 (45)	7 (28)	488 (49)	32 (39)	337 (50)	101 (53)
Race						
White	905 (95)	23 (92)	873 (87)	55 (67)	582 (87)	143 (75)
Other	43 (5)	2 (8)	132 (13)	27 (33)	90 (13)	47 (25)
Educational Level						
High school or less	116 (12)	8 (32)	112 (11)	28 (34)	62 (9)	37 (19)
More than high school	831 (88)	16 (64)	891 (89)	53 (64)	609 (91)	153 (81)
Annual income						
≤$24,999	535 (56)	16 (64)	582 (58)	57 (70)	379 (56)	128 (67)
>$25,000	335 (44)	4 (16)	368 (37)	14 (17)	258 (38)	46 (24)
Secondary Insurance						
Private	NC	NC	NC	NC	313 (38)	65 (34)
Medicaid	NC	NC	NC	NC	30 (4)	9 (5)
Other (VA, etc)	NC	NC	NC	NC	189 (28)	22 (12)
None	NC	NC	NC	NC	36 (5)	19 (10)
ADL score, mean (SD)	0.09(.38)	0.16(.47)	0.17(.56)	0.5(1.13)	0.41(.93)	1.63(2.03)

Abbreviations: NC, Not collected in this study year; ADL, Activities of daily living.

Investigating the effect of dementia on the use of chemoprophylaxis for CHD is the main empirical question in this research. To be included in the study sample, subjects had to be eligible for secondary chemoprevention for CHD sometime before or during 1999. While 100% of the sample developed CHD by 1999, subjects' status could vary each year among the following four categories: no CHD and no dementia, dementia only, CHD only, both dementia and CHD, or death. For example, during study year 5 (1992) 30.5% had no disease, 2.3% of the sample had dementia only, 62% had CHD only, and 5.2% had both diseases. By study year 11 (1999), 61.4% developed CHD, 17.3% developed both CHD and dementia, and 21.2% were dead. Figure 4.1 presents the distribution of disease states for each study year.

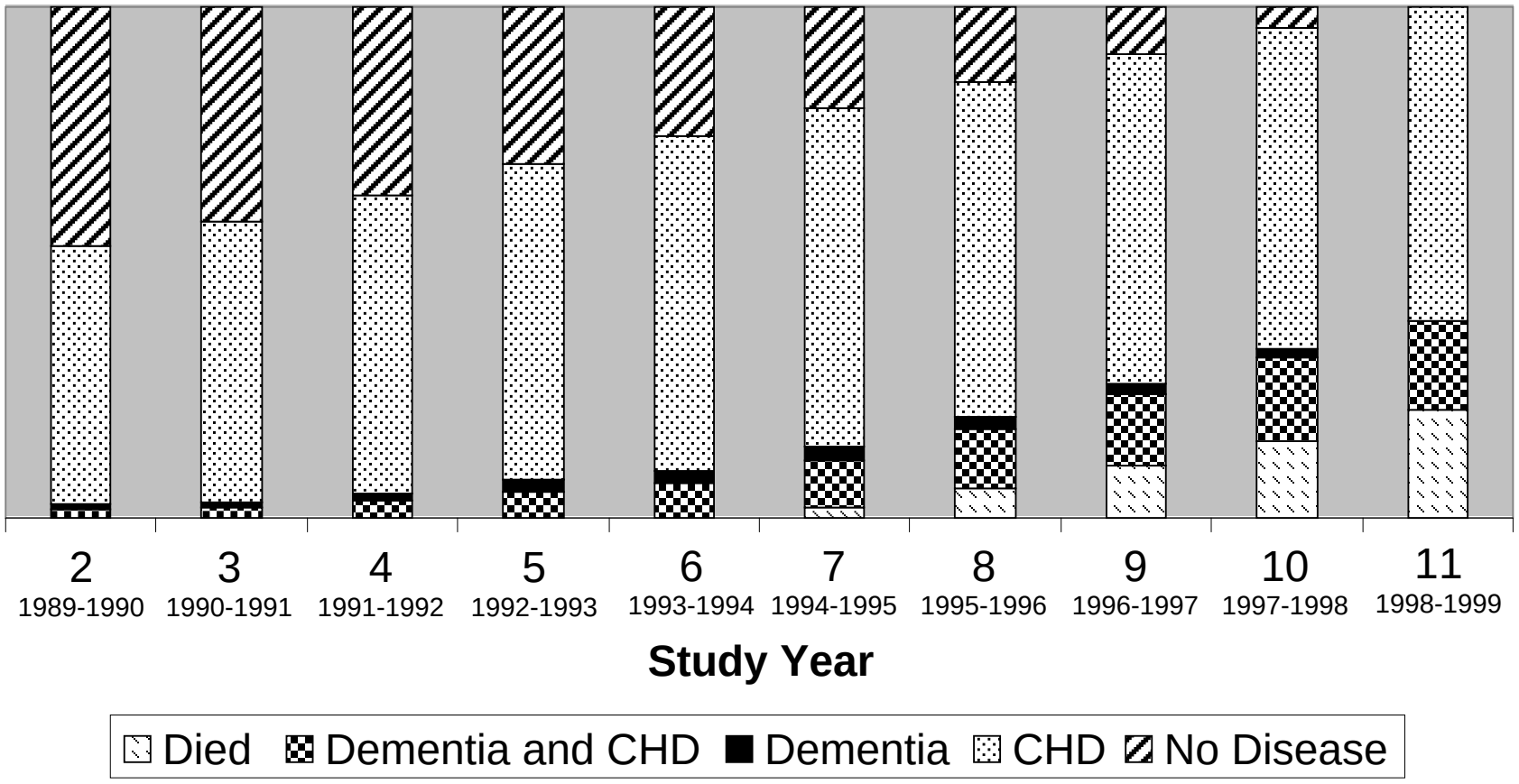


Figure 4.1: Disease states by year.

4.1.2 Dependent variables

The dependent variables for this study include four sub-classes of guideline-recommended chemoprophylaxis for CHD and two variables that measure compliance with chemoprophylaxis. Unadjusted rates of use of guideline-recommended chemoprophylaxis for CHD for representative years are presented in Table 4.2. Unadjusted rates show that there are differences in use and compliance for those with dementia compared to those without dementia. In earlier study years, participants with dementia were more likely to report taking ACE inhibitors and antiplatelet medications. In later years as the cohort ages, those with dementia are less likely to report taking any of the four classes of medication and are more likely to be non-compliant with all four classes of medication.

Table 4.2: Unadjusted use of chemoprophylaxis for CHD by dementia status in three representative study years, No.(%)

	1989		1992		1999	
VARIABLE	**Participants without Dementia (n=948)**	**Participants with Dementia (n=25)**	**Participants without Dementia (n=1005)**	**Participants with Dementia (n=82)**	**Participants without Dementia (n=672)**	**Participants with Dementia (n=190)**
ACE Inhibitors	62 (6.5)	3 (12)	131(13)	15 (18.3)	146 (21.7)	35 (18.4)
Beta-blockers	212 (22.3)	4 (16)	221(22)	8 (9.7)	220 (32.7)	36 (18.9)
Lipid-lowering medications [a]	65 (6.8)	1 (4)	102 (10.1)	3 (3.6)	184 (27.3)	22 (11.5)
Any antiplatelet medication [b]	421 (44.4)	15 (60)	527 (52.4)	39 (47.5)	373 (55.5)	72 (37.9)
0% compliant with chemoprophylaxis	378 (39.8)	8 (32)	319 (31.7)	32 (39)	88 (13.1)	40 (21)
50-100% compliant with chemoprophylaxis	168 (17.7)	6 (24)	266 (26.4)	15 (18.2)	300 (44.6)	50 (26.3)

Abbreviations: CHD, Coronary Heart Disease; ACE inhibitors, Angiotensin- Converting Enzyme Inhibitors.

[a] HMG0CoA Reductase Inhibitors

[b] Aspirin and other anti-platelet drugs

4.2 BIVARIATE RESULTS

The following section describes the first step of the model building process and results of the bivariate analyses, by study aim. For each study aim, the main independent variable, dementia status, could be measured a variety of ways. Tables 4.3, 4.5, and 4.7 present the results of possible specifications of dementia status for each aim.

Using the sampling weights that were created for each subject for each year based on the probability of each subject being missing for both cohorts, weighted and non-weighted bivariate analyses were conducted for the all variables. Variables that were significant predictors at $p \leq 0.1$ on the weighted bivariate analyses were retained for inclusion in the full multivariable model as were those that were not statistically significant, but important to the model based on theory and previous findings from the literature. Variables that were not significant predictors in the bivariate analyses, but were found to be confounding variables that produced a >10% change in the beta coefficients were included in the full models. All bivariate analyses were performed using STATA software version 10. Tables 4.4, 4.6, and 4.8 include the weighted bivariate results for study aims 1, 2 and 3, respectively. Appendix E contains results of the non-weighted bivariate analyses for each study aim.

4.2.1 Aim 1

4.2.1.1 Main independent variable

Study aim1 tests if Medicare beneficiaries with dementia and CHD less likely to take evidence-based chemoprophylaxis for CHD compared to those with CHD but without dementia. The analytical model uses ten years of longitudinal data on subjects (n=1087) who have CHD at entry or who develop it sometime during the study, and compares the subjects' use of chemoprophylaxis dependent on their dementia status.

For study aim 1, time of dementia onset as it relates to the onset of CHD, is not controlled for in the model. Potential specifications of how to measure dementia status for this aim include: (1) the clinically adjudicated date of onset determined by the CHS study, (2) the presence of dementia at baseline based on date of onset and year of entry into the study, (3) prevalent dementia (the static CHS determination of prevalence that spans the first three years of entry for each cohort), or (4) cognitive scores based on the 3MSE scores and (5) DSST scores. All possible specifications of dementia status were tested independently with each dependent variable with and without the sampling weights. Table 4.3 shows the results of the unadjusted, weighted bivariate GEE models for all possible specifications of dementia status for study aim 1. Appendix D.1 presents the non-weighted results.

Results from the weighted bivariate analyses do not yield that one consistent measure of dementia status is stronger at predicting the use of chemoprophylaxis. The CHS determination of prevalent dementia is a significant predictor for three of the six dependent variables (lipid-lowering medications, antiplatelet medications, and 50-100% compliance). A limitation of using this measure in the multivariable models is that it is a static variable that includes only those who

were determined by CHS to have dementia at entry into the study and does not accurately represent each subject's dementia status for each year or account for those in the sample who developed dementia during the study. Given this limitation and a lack of consistent statistical significance for any other measure, the choice of the primary measure of dementia status was made based on the strongest measure that matches the research question. The model for study aim 1 is testing whether those with dementia *at any time in the study* are less likely to use chemoprophylaxis than those without dementia. The dependent variable that captures "dementia status each year" (dementia present in that year) was selected as the primary independent variable for aim 1 because it accounts for dementia status each year, not just at entry, and is based on the clinically adjudicated date of onset. Sensitivity analyses for study aim 1 include a test of all alternative specifications full and final multivariable models.

Table 4.3: Results of weighted bivariate analyses for all possible specifications of dementia status for study aim 1

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid-Lowering Medications	Antiplatelet Medications	0% Compliance	50-100% Compliance
Dementia (present in that year)†	NS	NS	*(negative)	NS	NS	NS
Dementia at baseline	NS	NS	**(negative)	NS	NS	*(negative)
Prevalent Dementia	NS	NS	***(negative)	*(negative)	NS	*(negative)
3MSE Score Less than 80	NS	NS	**(negative)	NS	NS	*(negative)
DSST Score Less than 30	NS	NS	NS	NS	NS	NS

† Primary independent variable

Abbreviations: NS, not significant;3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test.

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.2.1.2 Control variables

The predisposing variables, as defined by the Andersen model, that were tested bivariately in both a weighted and non-weighted model include age, sex, race, and level of education. For some predisposing variables, such as age and education level, different log forms and alternative specifications were also analyzed to test the best functional form**.**

Participant age, when measured continuously centered at the mean, was significant for only antiplatelet medications at $p<0.1$ indicating that older subjects were less likely to report taking an antiplatelet medication. For both compliance variables age was significant at $p<0.05$ indicating that older patients were more likely to be 0% compliant with all four medications and younger subjects were more likely to be 50-100% compliant with all four medications.

Categories of age were also tested bivariately. For all chemoprophylaxis, with the exception of beta-blockers, those aged≥86 were less likely to report taking chemoprophylaxis and are the most likely to be 0% compliant with any of the four medications.

The bivariate results for sex match those for age in that it was only a significant predictor for use of antiplatelet medications. Female subjects were 0.03 times as likely to report taking an antiplatelet medication ($p\leq0.05$).

Race was a statistically significant predictor at $p<0.1$ for all medications, except for beta-blockers. Whites were more likely to report taking ACE inhibitors, lipid-lowering medications, and antiplatelet medications. The compliance variables confirmed this finding in that non-whites were more likely to report not taking any medications (0% compliant) and whites were more likely to report being compliant with at least two, three, or all four medications ($p\leq0.01$).

Level of education was tested as both a binary variable (less than high school) and as a categorical variable (less than high school, high school, more than high school). In the

unadjusted bivariate analyses, education was not a significant predictor of use for any of the four chemoprophylaxis or with the two compliance variables.

Three control variables that are included which are considered *enabling variables,* based on the Andersen model, include income, insurance status and nursing home residence. Income was only a slightly significant predictor for ACE inhibitors, but statistically significant for lipid-lowering medications among subjects with an income of less than $24,999 per year ($p<0.01$). Presence of supplementary insurance (to Medicare) was tested in two different ways: (1) as a categorical variable measuring supplemental insurance status each year and (2) as a binary variable measuring if a subject ever had a form of supplemental insurance. Insurance status was only collected in study year 6, 7, 9, 10, and 11, resulting in missing data for the other years. Including this variable in the GEE models dropped the number of analyzable observations by half, so it was not included in any of the full or final multivariable models. The binary measure of insurance status measured if a subject *ever* had a type of secondary insurance. Ever having private insurance was the only significant predictor at $p\leq0.1$ for antiplatelet medications. People living in a nursing home are 2.4 times as likely to report taking an ACE inhibitor, but are only 0.70 times as likely to report taking a beta-blocker, and 0.58 times as likely to report taking a lipid-lowering medication.

Control variables for aim 1 that measure comorbidites and the *level of care needed* include activities of daily living (ADLs), history of hypertension, diabetes, kidney disease, or ever having a diagnosis of cancer. Those needing more assistance with ADLs are more likely to report taking ACE inhibitors ($p\leq0.05$) and those with hypertension and diabetes are more likely to report taking a beta-blocker ($p\leq0.0001$) and lipid-lowering medication ($p\leq0.01$). Table 4.4

presents the coefficients and odds ratios (ORs) for the weighted bivariate analyses for each dependent variable. Appendix E.1 presents the non-weighted results.

Table 4.4: Results of weighted bivariate analyses of chemoprophylaxis for CHD in participants with dementia and CHD

Variable	ACE Inhibitors		Beta-blockers		Lipid-lowering Medications		Antiplatelet Medications	
Predisposing Variables	β coefficient	OR	β coefficient	OR	β coefficient	OR	β coefficient	OR
Dementia (in that year)	0.197	1.21	–0.067	0.93	–0.636*	0.52	–0.178	0.83
Dementia at baseline	0.878	0.41	–0.390	0.67	–1.591**	0.20	–0.224	0.79
Prevalent dementia	0.041	1.04	–0.518	0.59	–1.593***	0.20	0.593*	0.04
3MSE Score <=80	0.183	1.20	–0.077	0.92	–0.413**	0.66	0.800	0.15
DSST Score <=30	–0.106	0.89	–0.133	0.87	–0.154	0.85	0.838	0.15
Age centered on the mean	–0.003	0.99	–0.013	0.98	–0.001	0.99	0.979	0.14
Age categories (≤75)								
76-85	–0.133	0.87	–0.006	0.99	0.025	1.02	0.936	0.65
86-102	–0.522	0.59	0.049	1.05	–1.042***	0.35	0.647	0.07
Age and dementia interaction	–0.014	0.98	0.009	1.00	–0.017	0.98	0.993	0.75
Study site (North Carolina)	–0.229	0.80	0.050	1.05	–0.257	0.77	–0.103	0.90
California	–0.418	0.65	–0.757	0.46	–0.804**	0.44	–0.166	0.84
Maryland	–0.259	0.77	–0.416	0.65	–0.121	0.88	–0.309	0.73
Pennsylvania	–0.853*	0.42	0.076	1.07	–1.234***	0.29	–0.306	0.73
Race (white)	0.406	1.50	–0.156	0.85	0.512*	1.67	–2.08***	0.01
Gender (male)	0.217	1.24	0.258	1.29	–0.093	0.91	1.43*	0.03
Education (HS or less)	0.125	1.13	0.033	1.03	–0.212	0.80	0.988	0.89
Enabling Variables								
Income (<$24,999/year)	–0.389	0.67	–0.232	0.79	–0.296	0.74	0.631**	0.01
Insurance status (none)								
Private	0.055	1.05	0.071	1.07	0.163	1.17	0.100	1.10
Medicaid	–0.099	0 .90	–0.175	0.83	–0.420	0.65	–0.040	0.96
Other	0.147	1.15	0.094	1.09	0.198	1.21	0.025	1.02
Ever had private insurance	0.387	1.14	0.386	1.47	0.992	2.69	0.399	1.49
Ever had Medicaid	–0.037	0.96	–0.476	0.62	–1.691	0.93	–0.279	0.75
Ever had other insurance	0.284	1.32	–0.208	0.81	–0.024	0.97	–0.228	0.79
Ever without insurance	–0.240	0.78	–0.276	0.75	–0.010	0.98	–0.327	0.72
Residing in Nursing Home	0.911*	2.48	–0.250***	0.77	–0.537***	0.58	0.915	0.90
Care Need Variables								
Activities of Daily Living	0.086*	1.09	0.000	1.00	–0.031	0.96	0.902	0.09
Hypertension	0.111	1.11	0.124***	1.13	0.260**	1.29	1.01	0.72
Diabetes	0.173*	1.18	–0.120**	0.88	0.155	1.16	1.01	0.80
Renal Insufficiency	–0.162	0.85	0.327	1.38	–0.713	0.49	1.06	0.81
Ever treated for Cancer	0.236	1.26	0.488	1.63	–0.639	0.52	1.42	0.11

Abbreviations: 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test; CHD, Coronary Heart Disease.
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.2.2 Aim 2

4.2.2.1 Main independent variable

Study aim 2 tests if Medicare beneficiaries who develop dementia first then develop CHD less likely to take evidence-based chemoprophylaxis for CHD compared to those who develop CHD first then develop dementia. In this aim, the hypothesis is that the timing of disease onset has an effect on the use of chemoprophylaxis for CHD. The sample is limited to participants who develop both diseases by the end of the study (n=261) and the tests specifically if developing dementia first yields less use of chemoprophylaxis for CHD. Excluded from the analyses are participants who develop dementia and CHD in the same year including those with both diseases at baseline.

Possible measures of dementia status include specifications that model the time of onset of each disease. They include: (1) a static binary variable indicating if the year of onset for dementia is prior to the year of onset for CHD, (2) a categorical variable that measures disease status for both conditions in each study year (i.e. no disease, CHD only, dementia only, both diseases). This variable captures the time points in the study when participant become eligible to be in different comparison groups in the analysis, (3) the number of years since the dementia diagnosis, with year 1 at the year of onset. Table 4.5 presents the results of the unadjusted weighted bivariate analyses for all possible specifications of dementia status for aim 2. Appendix D.2 presents the non-weighted results.

Results from the weighted bivariate analysis indicate that the static binary measure of dementia status is a significant predictor for three of the six dependent variables (beta-blockers, lipid-lowering medication, and 0% compliance). Additionally, the categorical variable that

measures disease state each year is a strong predictor for all outcomes. Number of years since the dementia diagnosis was consistently not a significant predictor. Based on these results, the static binary measure of dementia status was selected as the main independent variable for aim 2. Additionally, the dynamic categorical variable was selected for inclusion in the multivariate model as a way to test any possible differences within the various categories (disease states). Included in the sensitivity analysis are all specifications, which were tested independently in the full and final models for aim 2.

Table 4.5: Results of weighted bivariate analyses for all possible specifications of dementia status for study aim 2

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid – lowering Medications	Antiplatelet Medications	0% Compliance	50-100% Compliance
Dementia before CHD †	NS	**(negative)	***(negative)	NS	***(positive)	NS
Disease status each year						
No disease (suppressed category)						
CHD only	NS	***(positive)	***(positive)	***(positive)	***(negative)	***(positive)
Dementia only	NS	NS	NS	**(positive)	**(negative)	***(positive)
Both diseases	*(positive)	**(positive)	**(positive)	***(positive)	***(negative)	***(positive)
No. of years since dementia diagnosis	NS	NS	NS	NS	NS	NS

† Primary independent variable
Abbreviations: NS, not significant; CHD, coronary heart disease.
P values: *p≤0.05;**p≤ 0.01;*** p≤ 0.001.

4.2.2.2 Control variables

Following the same methodology as outlined for aim 1 in Section 4.2.1.1, predisposing variables were tested bivariately in both a weighted and non-weighted models. They include age, sex, race, and level of education. Different log forms and specifications were tested for age and education level.

The interaction variable of participant age and dementia status is significant predictor for lipid-lowering medications at $p<0.01$. The bivariate results for sex and race indicate that non-whites are less likely to report taking an antiplatelet medication ($p<0.05$) while females are more likely ($p<0.05$).

Three control variables, that are considered enabling variables based on the Andersen model, include income, insurance status and nursing home residence. Income was not statistically significant predictor, but living in a nursing home was significant for ACE inhibitors, beta-blockers, and lipid-lowering medications ($p<0.05$) indicating that those living in a nursing home were more likely to report taking ACE inhibitors, but less likely to report taking a beta-blocker or lipid-lowering medication. Presence of supplementary insurance was tested in two different ways: (1) as a categorical variable measuring insurance status each year and (2) as a binary variable measuring if a subject ever had a form of secondary insurance (in addition to Medicare). The binary measure of insurance status measured if a subject *ever* had a type of secondary insurance. Ever having private insurance was the only significant predictor ($p<0.05$) for use of antiplatelet medications.

The control variables bivariately tested for aim 2 measure comorbidites and the level of care needed. They include activities of daily living (ADLs), history of hypertension, diabetes, kidney disease, or ever having a diagnosis of cancer. Those needing more assistance with ADLs

are more likely to report taking ACE inhibitors and antiplatelet medications, and those with hypertension are more likely to report taking a beta-blocker. Table 4.6 shows the coefficients and odds ratios (ORs) from the weighted bivariate analyses for each dependent variable. Appendix E.2 presents the non-weighted results.

Table 4.6: Results of weighted bivariate analysis of chemoprophylaxis for CHD for participants with dementia before CHD

Variable	ACE Inhibitors		Beta-blockers		Lipid-lowering Medications		Antiplatelet Medications	
Predisposing Variables	β coefficient	OR	β coefficient	OR	β coefficient	OR	β coefficient	OR
Dementia before CHD	–0.124	0.88	–1.810***	0.16	–3.005***	0.04	–0.632	0.53
Disease status each year (none)								
CHD only	1.146	3.14	2.191***	8.94	1.526***	4.60	1.573***	4.82
Dementia only	0.785	2.19	0.768	2.15	–0.222	0.80	3.070**	3.07
Both diseases	1.361*	3.90	2.040**	7.69	1.065**	2.90	1.614***	5.02
No. of years since dementia diagnosis	–0.124	0.08	–1.810	0.16	–0.008	0.99	0.003	1.00
Age centered on the mean	–0.012	0.98	0.004	1.00	–0.001	1.00	0.017	1.01
Age categories (≤75)								
76-85	–0.1461	0.86	0.087	1.09	0.068	1.07	0.190	1.20
86-102	–0.397	0.67	0.229	1.25	–0.864**	0.42	0.185	1.20
Age and dementia interaction	–0.040	0.96	–0.052	0.94	–0.082**	0.92	–0.010	0.98
Study site (North Carolina)								
California	–0.030	0.97	0.353	1.42	–0.662	0.52	0.271	1.31
Maryland	0.134	1.14	–0.007	0.99	1.293	3.65	0.116	1.12
Pennsylvania	–0.934	0.39	0.358	1.43	–0.291	0.74	0.007	1.00
Race (white)	0.757	2.13	–0.011	0.98	0.068	1.07	–0.916*	2.50
Gender (male)	0.338	1.40	–0.317	0.72	–0.493	0.61	0.636*	1.88
Education (HS or less)	0.257	1.29	0.165	1.17	–0.138	0.87	–0.125	0.88
Enabling Variables								
Income (≤$24,999/year)	–0.014	0.98	–0.406	0.66	0.083	1.08	–0.418	0.65
Insurance status (none)								
Private	0.113	1.12	0.207	1.23	0.025	1.02	0.096	1.10
Medicaid	0.275	1.31	–0.209	0.81	–0.333	0.71	–0.235	0.78
Other	0.092	1.09	0.177	1.19	–0.206	0.81	0.389	1.47
Ever had private insurance	0.313	1.36	0.785	2.19	2.292**	9.90	0.187	1.20
Ever had Medicaid	–0.126	0.88	–1.076**	0.34	1.285	3.61	0.043	1.04
Ever had other insurance	0.415	1.51	–0.672	0.51	–1.375*	0.25	0.077	1.08
Ever without insurance	–0.194	0.82	0.626	0.53	0.202	1.22	–0.519**	0.59
Residing in Nursing Home	0.987*	2.68	–0.294**	0.74	–0.384*	0.68	0.252	1.28
Care Need Variables								
Activities of Daily Living	0.085*	1.08	0.069	1.07	–0.107	0.89	–0.037	1.03
Hypertension	0.110	1.11	0.144*	1.15	–0.090	0.91	–0.050	0.95
Diabetes	0.235	1.26	0.063	1.06	–0.011	0.98	0.183	1.20
Renal Insufficiency	–0.100	0.90	0.475	1.60	–1.836**	0.16	–0.252	1.28
Ever treated for Cancer	0.874*	2.39	0.562	1.75	–1.720**	0.17	0.183	1.20

Abbreviations: CHD, Coronary Heart Disease; No., number; HS, high school. P values: ≤p 0.05; **p≤0 .01;*** p≤0.001.

4.2.3 Aim 3

4.2.3.1 Main independent variable

Study aim 3 tests if Medicare beneficiaries who develop CHD first are more likely to discontinue evidence-based chemoprophylaxis for CHD after they develop dementia. The sample for the analyses is limited to participants who develop dementia before CHD and who use chemoprophylaxis for at least one study year. Excluded from the analyses are participants who develop dementia before CHD, those who develop dementia and CHD in the same year (including those with both diseases at baseline), and the observations for participants before their first documented use of chemoprophylaxis (e.g. they must start to be eligible to discontinue).

The analysis is restricted to those who develop dementia after CHD, possible measures of dementia status include: (1) the number of years since the clinically adjudicated date of onset (with year of onset as "1"), (2) cognitive function scores based on the 3MSE scores, and (3) cognitive function scores based on DSST scores. All possible specifications of dementia status were tested independently with and without the sampling weights. The number of years since the dementia diagnosis is reported as the main measure for the multivariable models. Using this measure allows us to model the time with dementia as a possible indication of severity of disease. Table 4.7 presents the results of the weighted bivariate analyses for all possible specifications of dementia status for study aim 3. Appendix D.3 presents the non-weighted results.

Table 4.7: Results of weighted bivariate analyses for all possible specifications of dementia status for study aim 3

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid -lowering Medications	Antiplatelet Medications
No. of years since dementia diagnosis †	NS	NS	**(negative)	**(negative)
3MSE Score Less than 80	NS	NS	NS	**(negative)
DSST Score Less than 30	NS	NS	**(negative)	NS

† Primary independent variable

Abbreviations: NS, not significant; 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test.

P values: P values: *p≤0.05;**p≤ 0.01;*** p≤ 0.001.

4.2.3.2 Control variables

Predisposing variables were tested bivariately in both a weighted and non-weighted models. They include age, sex, race, and level of education. Different log forms and specifications were tested for age and education level.

Participant age, when measured continuously centered at the mean, was not a significant predictor for use of chemoprophylaxis. Participants ≥86 years old were 0.52 as likely to report taking a lipid-lowering medication ($p \leq 0.001$).

Results for race indicate that non-whites are less likely to report taking an ACE inhibitor and antiplatelet medication ($p<0.05$) while females are more likely. Gender and level of education were statistically significant predictor for use of antiplatelet medications ($p \leq 0.001$).

Three enabling variables controlled for in the model include income, insurance status and nursing home residence. Income statistically predicted use of antiplatelets. Participants living in a nursing home were three times as likely to report taking an ACE inhibitor and 0.86 as likely to report taking an lipid-lowering medication ($p \leq 0.05$). Supplemental insurance was tested two different ways in the bivariate analysis: as a categorical variable measuring insurance status each year and as a binary variable measuring if a subject ever had some form of supplementary insurance. Given the amount of missing data for the categorical variable it was not included in any of the full multivariable models. Ever having private insurance or ever having Medicaid were significant predictors for use of lipid-lowering medications at $p \leq 0.001$.

Control variables measuring comorbidites and the level of care needed include activities of daily living (ADLs), history of hypertension, diabetes, kidney disease, or ever having a diagnosis of cancer. Also included was a variable that controlled for the number of years with CHD. This variable is important to control for effect of length of disease on use of

chemoprophylaxis. For all four sub-classes of medications, the longer the amount of time with CHD the less likely to report using the medication. Participants with kidney disease and a history of cancer were less likely to report taking a lipid-lowering medication ($p \leq 0.01$). Table 4.8 displays the coefficients and odds ratios (ORs) from the weighted bivariate analyses for each dependent variable. Appendix E.3 includes the non-weighted results.

Table 4.8: Results of weighted bivariate analysis of chemoprophylaxis for CHD in participants with CHD before dementia

Variable	ACE Inhibitors		Beta-blockers		Lipid-lowering Medications		Antiplatelet Medications	
Predisposing Variables	β coefficient	OR	β coefficient	OR	β coefficient	OR	β coefficient	OR
No. of yrs since dementia	–0.270	0.76	–0.233	0.79	–0.467**	0.62	–0.336***	0.71
3MSE Score <=80	–0.971	0.38	0.030	1.03	–1.352	0.26	–0.994**	0.37
DSST Score <=30	–2.505	0.08	–0.035	0.96	–1.870**	0.15	–0.120	0.89
Age centered on the mean	–0.141	0.87	–0.122*	0.88	0.208	1.02	–0.064*	0.94
Age categories 76-85	–0.120	0.89	0.055	1.06	0.110	1.12	–0.197	0.82
86-102	–1.771*	0.17	–0.894	0.41	–0.984	0.37	–0.409	0.66
Age and yrs since dementia interaction	–0.042*	0.95	–0.030*	0.97	0.016	1.01	–0.025**	0.98
Age and dementia interaction	–0.135*	0.87	–0.028	0.97	0.173	1.19	–0.089***	0.92
Study Site (North Carolina)								
California	1.181	3.26	–2.114**	0.12	0.127**	1.14	–0.882	0.92
Maryland	1.131*	3.10	–1.739*	0.18	2.314	10.12	0.354	1.43
Pennsylvania	0.754	2.13	–1.382	0.25	0.186	1.91	0.177	1.19
Race (white)	0.049	1.05	–1.326	0.27	2.020**	7.53	0.677*	1.97
Gender (male)	0.608	1.84	0.093	1.10	1.750*	5.75	0.194	1.21
Education (HS or less)	0.745	2.11	–0.429	0.65	–1.000	0.37	–0.229	0.80
Enabling Variables								
Income (<$24,999/year)	0.370	1.45	–0.361	0.70	–0.627	0.53	–0.853**	0.43
Insurance status								
Private	0.152	1.16	0.172	1.19	–0.457	0.64	0.525	1.69
Medicaid	–0.383	0.68	–0.085	0.92	0.973*	2.65	0.560	1.75
Other	0.775	2.17	0.147	1.16	–0.174	0.84	0.764	2.15
Ever had private insurance	0.088	1.09	0.434	1.54	1.526**	4.60	0.239	1.27
Ever had Medicaid	–0.707	0.49	–0.256	0.77	2.907*	18.29	–0.585	0.56
Ever had other insurance	0.683	1.98	–0.554	0.57	–0.579	0.56	0.058	1.06
Ever had no secondary ins	–0.415	0.66	–0.174	0.84	0.838	2.31	–0.452	0.64
Residing in Nursing Home	–0.233	0.80	–0.380	0.68	–0.567	0.56	–1.293	0.27
Care Need Variables								
Activities of Daily Living	0.193	1.21	–0.193***	0.82	–0.294**	0.75	–0.217*	0.80
No. of yrs since CHD	–0.192*	0.83	–0.262***	0.77	–0.161**	0.85	–0.220***	0.80
Hypertension	0.127	1.13	0.032	1.03	–-0.254	0.76	–0.063	0.94
Diabetes	0.313	1.37	–0.184	0.83	0.311	1.36	–0.124	0.88
Renal Insufficiency	0.352	1.42	0.310	1.36	–0.722	0.49	–0.218	0.80
Ever treated for Cancer	0.106	1.11	0.866	2.38	0.297	1.35	0.225	1.25
Any arthritis	–0.048	0.95	0.680	1.97	–0.915	0.40	0.227	1.25

Abbreviations: 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test; CHD, Coronary Heart Disease; No, number.
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3 MULTIVARIABLE RESULTS

4.3.1 Aim 1

Study aim1 tests if Medicare beneficiaries with dementia *and* CHD less likely to take evidence-based chemoprophylaxis for CHD compared to those with CHD but without dementia. Multivariable analyses for study aim 1 included weighted generalized estimating equations (GEE) models for four chemoprophylaxis dependent variables (ACE inhibitors, beta-blockers, lipid-lowering medications, and antiplatelet medications) and two measures of compliance with chemoprophylaxis (0% compliance for those who have CHD and do not report taking any of the medications and 50-100% compliance for those with CHD who report taking at least two, three or all four). Odds ratios (ORs) and accompanying 95% confidence intervals (CI) were calculated to represent the strength of association between use of chemoprophylaxis and the presence of dementia.

The GEE method was used to account for the repeated measures of the longitudinal data on the exposure of interest (dementia status) and outcomes (chemoprophylaxis use). Each model includes sample weights to adjust the probability of being in either of the two cohorts recruited in two different study years.

The full multivariable model for aim 1 includes 17 variables (independent and control) for ACE inhibitors, beta-blockers and lipid-lowering medication, and 18 variable for antiplatelet and the compliance dependent variables. The predisposing variables include age, dementia and age interaction, sex, race, study site, and level of education (above or below high school).

Enabling variables included income, insurance status, and residing in a nursing home. The full multivariate models also control for care needs (functional status and co-morbidities) including, activities of daily living (ADLs), history of hypertension, diabetes or kidney disease. The antiplatelet and compliance models additionally control for arthritis as a comorbid condition. All of the variables were forced into the logistical GEE models for each medication sub-class and for the two measures of compliance measures. The following sections describe the results of the full and final multivariable models for study aim 1.

4.3.1.1 ACE inhibitors

Using the full multivariable logistic GEE model, there was no statistically significant differences in the use of ACE inhibitors between those with and without dementia. Having private supplemental insurance to Medicare as was the only control variable that significantly predicted use of ACE inhibitors ($p \leq 0.05$; OR=2.11; 95% CI =1.02-4.37).

To create the final model, variables were added into the unadjusted model one at a time. They were selected if they were $p \leq 0.1$ on the bivariate analyses, were theoretically important, or if they were confounding and yielded a >10% difference on the dementia coefficient between the unadjusted model and the crude model.

The final model for ACE inhibitors controlled for age, race, sex, study site, and a dementia and age interaction variable. Results do not support the hypothesis that those with dementia are less likely to report taking an ACE inhibitor (p=0.06). The Pennsylvania study site was the only control variable in the final model that significantly predicted less use of ACE inhibitors ($p \leq 0.05$; OR=0.45; 95% CI= 0.23-0.88). Table 4.9 presents the results of the full and final analyses for the use of ACE inhibitors among those with and without dementia.

Table 4.9: Multivariable results for use of ACE inhibitors for participants with CHD and dementia

Variable	ACE Inhibitors					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia (in that year)	0.170	1.18	0.77-1.80	0.380	1.45	0.97-2.16
Age (centered)	0.017	1.01	0.97-1.06	0.003	1.00	0.96-1.04
Age and dementia interaction	–0.019	0.98	0.93-1.02	–0.043	0.95	0.90-1.01
Study site (North Carolina)						
California	–0.219	0.80	0.36-1.75	–0.394	0.67	0.36-1.25
Maryland	0.148	1.15	0.58-2.29	–0.277	0.76	0.40-1.41
Pennsylvania	–0.613	0.54	0.24-1.18	–0.800*	0.45	0.23-0.88
Race (white)	0.248	1.28	0.61-2.65	0.330	1.40	0.71-2.70
Gender (male)	0.077	1.08	0.65-1.78	0.176	1.19	0.74-1.91
Educational Level (HS or less)	0.216	1.24	0.72-2.12			
Enabling Variables						
Income (≤$24,999)	–0.108	0.89	0.49-1.61			
Ever had private insurance	0.750*	2.11	1.02-4.37			
Ever had Medicaid	0.212	1.23	0.62-2.44			
Ever had other insurance	0.260	1.23	0.79-2.10			
Ever without insurance	0.203	1.29	0.65-2.30			
Residing in a Nursing Home	0.358	1.43	0.71-2.86			
Care Need Variables						
Activities of daily living	0.084	1.08	0.95-1.24			
Hypertension	0.054	1.05	0.90-1.22			
Diabetes	0.169	1.18	0.95-1.47			
Renal insufficiency	–0.428	0.65	0.34-1.23			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.1.2 Beta-blockers

The effect of dementia on the use of beta-blockers was assessed using a weighted GEE model. The full theoretical model included 17 predisposing, enabling and care need variables. There was no statistically significant difference in use of beta-blockers among those with and without dementia. Four control variable in the full model significantly predicted use of beta-blockers. Participants from the California(as compared to those in North Carolina) were less likely to report use ($p \leq 0.001$; OR=0.28; 95% CI=0.14 -0.58) as were those living in a nursing home ($p \leq 0.05$; OR=0.53; 95% CI=0.30-0.92), and those with diabetes ($p \leq 0.01$; OR=0.85; 95% CI=0.77-0.95). Participants with a history of hypertension were more likely to report taking a beta-blocker ($p \leq 0.001$; OR=1.15; 95% CI=1.08-1.23). These findings are consistent with CPGs that recommend, based on the evidence, that people with hypertension should take a beta-blocker, irrespective of their CHD status (VA/DoD, 2004) yet there is no evidence to support that those with diabetes and CHD benefit from a beta-blocker (Kaiser Permanente Care Management Institute, 2005).

The final model for beta-blockers controlled for age, race, sex, study site, an age and dementia interaction variable, and hypertension. Table 4.10 presents the coefficients, ORs, and CIs for the full theoretical and final model for use of beta-blocker.

Table 4.10: Multivariable results for use of beta-blockers for participants with CHD and dementia

Variable	Beta-blockers					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia (in that year)	0.801	1.08	0.60-1.93	–0.064	0.94	0.62-1.41
Age (centered)	–0.000	1.00	0.96-1.04	–0.016	0.98	0.94-1.02
Age and dementia interaction	0.001	1.00	0.94-1.06	0.033	1.03	0.98-1.08
Study site (North Carolina)						
California	–1.247***	0.28	0.14-0.58	–0.583	0.56	0.24-1.27
Maryland	–0.617	0.53	0.24-1.19	–0.400	0.70	0.29-1.53
Pennsylvania	–0.547	0.57	0.25-1.29	0.078	1.08	0.46-2.51
Race (white)	–0.396	0.67	0.30-1.47	0.089	0.91	0.43-1.91
Gender (male)	0.168	1.18	0.66-2.10	0.291	1.33	0.77-2.30
Educational Level (HS or less)	0.088	1.09	0.45-1.58			
Enabling Variables						
Income (≤$24,999)	–0.167	0.84	0.45-1.58			
Ever had private insurance	0.143	1.15	0.48-2.75			
Ever had Medicaid	–0.575	0.56	0.24-1.28			
Ever had other insurance	–0.255	0.77	0.48-1.24			
Ever without insurance	–0.229	0.79	0.37-1.68			
Residing in a Nursing Home	–0.632*	0.53	0.30-0.92			
Care Need Variables						
Activities of daily living	0.042	1.04	0.90-1.20			
Hypertension	0.145***	1.15	1.08-1.23	0.135***	1.14	1.07-1.22
Diabetes	–0.154**	0.85	0.77-0.95			
Renal insufficiency	0.458	1.58	0.77-3.21			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.1.3 Lipid-lowering medications

Included in the full multivariate model for lipid-lowering medications are all 17 independent, control and interaction variables. Results for the main independent variable in the full model show that participants with dementia are less likely to report taking a lipid-lowering medication, although not statistically significant. Variables that significantly predict lower rates of use of lipid-lowering medications in the full model include study site, California ($p \leq 0.01$; OR=0.34; 95% CI=0.17-0.69), and Pennsylvania ($p \leq 0.001$; OR=0.24; 95% CI=0.11 -0.50) compared to North Carolina, and living in a nursing home ($p \leq 0.05$; OR=0.37; 95% CI=0.17 -0.81). Control variables that significantly predicted more use of lipid-lowering medications include white race ($p \leq 0.05$; OR=2.18; 95% CI=1.06-4.47), private supplemental insurance ($p \leq 0.01$; OR=4.08; 95% CI=1.41-11.77), or no supplemental insurance sometime during the study ($p \leq 0.01$; OR=2.93; 95% CI=1.27-6.75), and a history of hypertension ($p \leq 0.01$; OR=1.43; 95% CI=1.10-1.86).

The final predictive model controlled for age, race, sex, study site, an interaction variable for age and dementia. Dementia significantly predicted less use of lipid-lowering medications ($p \leq 0.05$; OR=0.38; 95% CI=0.16-0.90), as well as the California ($p \leq 0.01$; OR=0.40; 95% CI=0.21-0.73) and Pennsylvania ($p \leq 0.001$; OR=0.26; 95% CI=0.13-0.50) study sites. The results support the hypothesis that those with dementia are less likely to report taking a lipid-lowering medication ($p \leq 0.05$). Table 4.11 presents the results for the full theoretical and final predictive model for lipid-lowering medications.

Table 4.11: Multivariable results for use of lipid-lowering medications for participants with CHD and dementia

Variable	Lipid-lowering Medications					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia (in that year)	–0.135	0.87	0.46-1.62	–0.945*	0.38	0.16-0.90
Age (centered)	–0.017	0.98	0.92-1.03	0.001	1.00	0.95-1.04
Age and dementia interaction	–0.013	0.98	0.92-1.04	0.050	1.05	0.96-1.14
Study site (North Carolina)						
California	–1.060**	0.34	0.17-0.69	–0.927**	0.39	0.21-0.73
Maryland	0.018	1.01	0.42-2.43	–0.211	0.81	0.36-1.80
Pennsylvania	–1.427***	0.24	0.11-0.50	–1.350***	0.26	0.13-0.50
Race (white)	0.781*	2.18	1.06-4.47	0.091	1.10	0.59-2.02
Gender (male)	–0.078	0.92	0.48-1.76	–0.144	0.86	0.47-1.56
Educational Level (HS or less)	–0.545	0.57	0.29-1.12			
Enabling Variables						
Income (≤$24,999)	–0.269	0.76	0.38-1.51			
Ever had private insurance	1.406**	4.08	1.41-11.77			
Ever had Medicaid	0.292	1.33	0.41-4.29			
Ever had other insurance	–0.189	0.82	0.44-1.52			
Ever without insurance	1.077**	2.93	1.27-6.75			
Residing in a Nursing Home	–0.985*	0.37	0.17-0.81			
Care Need Variables						
Activities of daily living	0.024	1.02	0.83-1.25			
Hypertension	0.363**	1.43	1.10-1.86			
Diabetes	0.182	1.20	0.98-1.46			
Renal insufficiency	–0.768	0.46	0.17-1.21			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.1.4 Antiplatelet medications

The full theoretical model for antiplatelet medications controlled for 18 predisposing, enabling, and care need variables. This includes all of the variables included in the ACE inhibitors, beta-blockers and lipid-lowering models (17) with the addition of a variable that controls for any form of arthritis since aspirin is a common medication used to treat the symptoms of arthritis. In the full model, dementia did not significantly predict the use of antiplatelet medications.

Variables that significantly predicted less use of antiplatelet medications in the full model include age ($p \leq 0.05$; OR=0.96; 95% CI=0.93 -0.99), Maryland study site (compared to North Carolina) $p \leq 0.05$; OR=0.55; 95% CI=0.32 -0.93), and needing more assistance with activities of daily living $p \leq 0.05$; OR=0.87; 95% CI=0.77 -0.99).

Variables that significantly predicted more use of antiplatelet medications in the full model the interaction between age and dementia ($p \leq 0.05$; OR=1.07; 95% CI=1.00 -1.15), white race ($p \leq 0.05$; OR=1.73; 95% CI=1.03-2.92), and a history of hypertension ($p \leq 0.05$; OR=1.16; 95% CI=1.01 -1.33).

To create the final model, variables were added into the unadjusted model one at a time. They were selected if they were $p \leq 0.1$ on the bivariate analyses, were theoretically important, or if they were confounding and yielded a >10% difference on the dementia coefficient between the unadjusted model and the crude model.

History of arthritis measure was forced into the final model. Control variables that significantly predicted higher use of antiplatelet medication include white race ($p \leq 0.01$; OR=2.00; 95% CI 1.25 -3.17). Older participants were less likely to report taking an antiplatelet

medication ($p \leq 0.01$; OR=0.96; 95% CI=0.93-0.97). Table 4.12 provides the coefficients, ORs, and CIs for the full and final models for antiplatelet medications.

Table 4.12: Multivariable results for use of antiplatelet medications for participants with CHD and dementia

Variable	Antiplatelet Medications					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia (in that year)	0.018	1.01	0.57-1.80	–0.061	0.95	0.61-1.45
Age (centered)	–0.039*	0.96	0.93-0.99	–0.044**	0.94	0.93-0.97
Age and dementia interaction	0.077*	1.07	1.00-1.15	0.001	1.00	0.91-1.10
Study site (North Carolina)						
California	–0.442	0.64	0.37-1.09	–0397	0.67	0.50-1.27
Maryland	–0.591*	0.55	0.32-0.93	–0.562	0.56	0.40-1.03
Pennsylvania	–0.315	0.72	0.42-1.15	–0.370	0.70	0.47-1.20
Race (white)	0.551*	1.73	1.03-2.92	0.691**	2.00	1.25-3.17
Gender (male)	0.319	1.37	0.94-2.00	0.164	1.20	0.84-1.65
Educational Level (HS or less)	–0.029	0.97	0.64-1.45			
Enabling Variables						
Income (≤$24,999)	–0.279	0.75	0.49-1.216			
Ever had private insurance	0.233	1.26	0.71-2.22			
Ever had Medicaid	0.160	1.17	0.71-1.91			
Ever had other insurance	–0.342	0.71	0.51-1.39			
Ever without insurance	–0.166	0.985	0.51-1.39			
Residing in a Nursing Home	0.832	2.29	0.11-49.14			
Care Need Variables						
Activities of daily living	–0.136*	0.87	0.77-0.99			
Hypertension	0.149*	1.16	1.01-1.33			
Diabetes	0.092	1.08	0.92-1.27			
Renal insufficiency	–0.131	0.87	0.51-1.48			
Any arthritis	0.046	1.04	0.81-1.35	–0.001	1.00	0.79-1.25

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.1.5 Compliance with medications

In addition to the four sub-classes of guideline-recommended chemoprophylaxis, two additional dependent variables were tested that measure compliance with chemoprophylaxis. One measure labeled participants as non-compliant (0%) if they had CHD but did not report taking any of the four mediations. The second approach was to label people as at least 50% compliant or greater if they had CHD and reported taking two, three or all four of the medications. Similar to the antiplatelet model, the full compliance models included 18 independent, control and interaction variables. Dementia status did not statistically predict compliance in the full model testing 0% compliance. Participants at the California study site were significantly more likely to be 0% non-compliant ($p \leq 0.05$; OR=1.75; 95% CI=1.00-3.07) as were those who reported having some form of supplemental insurance during the study ($p \leq 0.05$; OR=1.52; 95% CI=1.02 -2.27). White race ($p \leq 0.01$; OR=0.40; 95% CI=0.22-0.72), history of hypertension ($p \leq 0.001$; OR=0.77; 95% CI=0.64-0.87), and having private insurance at some point during the study significantly predicated a lesser likelihood of being 0% compliant) ($p \leq 0.05$; OR=1.04; 95% CI=1.01-1.07).

Dementia status did not statistically predict compliance in the full model testing 50-100% compliance. Participants at the California study site ($p \leq 0.01$; OR=0.40; 95% CI=0.21-0.78) and Pittsburgh ($p \leq 0.05$; OR=0.42; 95% CI=0.21-0.83) study site were significantly less likely to be 50-100% compliant compared to those from North Carolina. Participants with a history of hypertension were more likely to be 50%-100% compliant with chemoprophylaxis ($p \leq 0.001$; OR=1.22; 95% CI=1.09-1.37).

The final predictive models for compliance control for age, race, sex, site, age and dementia interaction and a history of hypertension. In the final model predicting 0% compliance, dementia status did not significantly predict compliance, although results indicate that those who

are older ($p \leq 0.05$; OR=1.04; 95% CI=1.01-1.07) and from the California study site ($p \leq 0.05$; OR=2.00; 95% CI=1.16-3.33) and Maryland study site ($p \leq 0.05$; OR=1.70; 95% CI=1.00-2.85) sites are more likely to be 0% compliant with chemoprophylaxis. White race ($p \leq 0.001$; OR=0.36; 95% CI=0.22-0.58) and a history of hypertension ($p \leq 0.0001$; OR=0.76; 95% CI=0.67-0.88) significantly predicted a lower likelihood of being 0% compliant.

Dementia status significantly predicated compliance in the final model for ≥50% compliance. Those with dementia and CHD are 0.60 as likely to be 50%-100% compliant with chemoprophylaxis compared to those without dementia ($p \leq 0.05$), controlling for age, sex, age and dementia interaction, study site and a history of hypertension. White race ($p \leq 0.05$; OR=1.86; 95% CI=1.07-3.24), the interaction between age and dementia ($p \leq 0.001$; OR=1.20; 95% CI 1.02-1.17), and a history of hypertension ($p \leq 0.001$; OR=1.16; 95% CI=1.05-1.31) significantly predicated higher likelihood of being 50%-100% compliant. The Pennsylvania study site compared to North Carolina ($p \leq 0.001$; OR=0.52; 95% CI=0.27-0.98) significantly predicted a lower likelihood of being 50%-100% compliant. Tables 4.13 and 4.14 present the results for the full theoretical model and final predictive models for 0% compliance and 50-100% compliance.

Table 4.13: Multivariable results of 0% compliance with chemoprophylaxis for participants with CHD and dementia

Variable	0% Compliance					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia (in that year)	–0.221	0.70	0.37-1.69	0.115	1.12	0.62-2.02
Age (centered)	0.025	1.02	0.99-1.06	0.040*	1.04	1.00-1.07
Age and dementia interaction	–0.007	1.00	0.91-1.08	–0.019	0.98	0.91-1.05
Study site (North Carolina)						
California	0.560*	1.75	1.00-3.07	0.677**	1.97	1.16-3.33
Maryland	0.303	1.35	0.77-2.35	0.523*	1.68	0.99-2.85
Pennsylvania	0.131	1.13	0.65-1.97	0.276	1.31	0.76-2.26
Race (white)	–0.907**	0.40	0.22-0.72	–1.021***	0.36	0.91-1.05
Gender (male)	–0.141	0.87	0.57-1.31	–0.179	0.84	0.56-1.23
Educational Level (HS or less)	–0.041	0.99	0.62-1.50			
Enabling Variables						
Income (≤$24,999)	0.223	1.25	0.77-2.02			
Ever had private insurance	–0.606*	0.54	0.31-0.97			
Ever had Medicaid	–0.139	0.87	0.51-1.48			
Ever had other insurance	0.422*	1.52	1.02-2.27			
Ever without insurance	–0.101	0.90	0.50-1.61			
Residing in a Nursing Home	–0.165	0.85	0.05-14.46			
Care Need Variables						
Activities of daily living	–0.006	0.99	0.82-1.19			
Hypertension	–0.289***	0.77	0.64-0.87	–0.265***	0.76	0.67-0.88
Diabetes	–0.135	0.87	0.71-1.08			
Renal insufficiency	0.204	1.22	0.64-2.33			
Any arthritis	–0.144	0.97	0.88-1.05			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

Table 4.14: Multivariable results of 50-100% compliance with chemoprophylaxis for participants with CHD and dementia

Variable	50-100% Compliance					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia (in that year)	–0.208	0.81	0.44-1.50	–0.520*	0.60	0.35-0.99
Age (centered)	–0.022	0.97	0.94-1.01	–0.035	0.97	0.92-1.00
Age and dementia interaction	0.051	1.05	0.97-1.13	0.94**	1.10	1.02-1.17
Study site (North Carolina)						
California	–0.907**	0.40	021-0.78	–0.598	0.55	0.29-1.03
Maryland	–0.378	0.68	0.35-1.30	–0.370	0.70	0.37-1.27
Pennsylvania	–0.870*	0.42	0.21-0.83	–0.654*	0.52	0.27-0.98
Race (white)	0.335	1.40	0.68-2.83	0.625*	1.86	1.07-3.24
Gender (male)	0.203	1.22	0.76-1.97	0.192	1.21	0.78-1.86
Educational Level (HS or less)	–0.090	0.91	0.54-1.51			
Enabling Variables						
Income (≤$24,999)	–0.162	0.85	0.50-1.44			
Ever had private insurance	0.598	1.81	0.94-3.50			
Ever had Medicaid	–0.249	0.78	0.36-1.68			
Ever had other insurance	–0.340	0.71	0.47-1.07			
Ever without insurance	0.415	1.451	0.83-2.75			
Residing in a Nursing Home	0.723	2.106	0.48-8.81			
Care Need Variables						
Activities of daily living	0.031	1.03	0.91-1.16			
Hypertension	0.203***	1.22	1.09-1.37	0.161***	1.18	1.05-1.31
Diabetes	0.134	1.14	0.96-1.36			
Renal insufficiency	–0.180	0.83	0.45-1.55			
Any arthritis	0.052	1.13	0.90-1.43			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001

4.3.1.6 Alternative specifications of main independent variable aim 1

The primary models for study aim 1 used the binary variable measuring dementia status in each year (yes or no) as the main independent variable. The determination of dementia was based on the clinically adjudicated date of onset by the CHS study. Once a participant was coded as having dementia (year of onset) they remained in that state until death or the end of the study. Two similar binary measures of dementia status were tested in a sensitivity analysis of the main models. The first was a binary measure of dementia of the Alzheimer's type and the second for vascular dementia. In final predictive models controlling for age, sex, race, and dementia and age interaction, vascular dementia significantly predicted use of three sub-classes of chemoprophylaxis. Dementia of the Alzheimer's type did not significantly predict use. Those with vascular dementia were more likely to report use of ACE inhibitors ($p \leq 0.001$; OR=4.76; 95% CI=1.64-13.78), and less likely to report use of beta-blockers ($p \leq 0.05$; OR=0.48; 95% CI=0.26-0.87), lipid-lowering medications ($p \leq 0.0001$; OR=0.21; 95% CI=0.93 -0.46). These results are interesting in that appears type of dementia may have a particular effect on use of chemoprophylaxis. For those with CHD and Alzheimer's disease, dementia did not have an effect. For those with CHD and vascular dementia, the presence of dementia predicted the use of chemoprophylaxis.

As described section 4.2.1.1 alternative forms of measuring dementia status were tested for aim 1. These include: dementia at baseline, prevalent dementia, 3MSE score <80, and DSST score < 30. Each alternative specification was tested in the full theoretical model and final predictive model. Table 4.15 presents the results of the alternative specifications of dementia for each model. Odds ratios and 95% confidence intervals for these models can be found in

Appendix F. An important finding is that results from the primary models do not vary from the model results using the alternative specification of dementia status.

Table 4.15: Multivariable results of alternative specifications of independent variable for aim 1

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid-Lowering Medications	Antiplatelet Medications	0% Compliance	50-100% Compliance
Full Model						
Dementia (in that year)†	NS	NS	NS	NS	NS	NS
AD Dementia (in that year)	NS	NS	NS	NS	NS	NS
Va Dementia (in that year)	NS	NS	NS	NS	NS	NS
Dementia at baseline	NS	NS	NS	NS	NS	NS
Prevalent Dementia	NS	NS	**(negative)	NS	NS	NS
3MSE Score Less than 80	NS	NS	**(negative)	NS	NS	*(negative)
DSST Score Less than 30	NS	NS	NS	NS	*(positive)	NS
Final Model						
Dementia (in that year) †	NS	NS	*(negative)	NS	NS	*(negative)
AD Dementia (in that year)	NS	NS	NS	NS	NS	NS
Va Dementia (in that year)	**(positive)	*(negative)	***(negative)	NS	NS	NS
Dementia at baseline	NS	NS	**(negative)	*(positive)	NS	*(negative)
Prevalent Dementia	NS	NS	***(negative)	NS	NS	**(negative)
3MSE Score Less than 80	NS	NS	**(negative)	NS	NS	NS
DSST Score Less than 30	NS	NS	NS	NS	NS	NS

† Primary independent variable

Abbreviations: AD, Alzheimer's disease; Va, Vascular, NS, not significant; 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test.

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.2 Aim 2

Multivariable analyses for study aim 2 include weighted, generalized estimating equations (GEE) for ACE inhibitors, beta-blockers, lipid-lowering medications, antiplatelet medications and for compliance with chemoprophylaxis to test if Medicare beneficiaries who develop dementia *before* CHD are less likely to take evidence-based chemoprophylaxis for CHD compared to those who develop dementia *after* CHD. Odds ratios (ORs) and accompanying 95% confidence intervals (CI) were calculated to represent the strength of association between use of chemoprophylaxis and timing of the onset of dementia in relation to the onset of CHD.

The full models for ACE inhibitors, beta-blockers and lipid-lowering medications controlled for 18 independent, control and interaction variables. The antiplatelet and compliance models included for 19 dependent variables. The predisposing variables include age, gender, race, level of education (above or below high school), study site, and age and dementia interaction, enabling variables include income, insurance status, and residing in a nursing home. The GEE models also control for other co-morbidities and care needs including, activities of daily living (ADLs), the presence of hypertension, diabetes or kidney disease and arthritis for the antiplatelet and compliance models. All of these variables were forced into the logistical GEE models for each class of chemoprophylaxis and for two measures of compliance with the medications.

4.3.2.1 ACE inhibitors

In the full model, the onset of dementia before CHD did not significantly predict use of ACE inhibitors. Additionally, no control variables in the model were statistically significant predictors.

To build the final predictive model, control variables that had a >10% confounding effect or were $p \leq 0.1$ on the bivariate analyses or were theoretically important (e.g. age) were added into the model one by one. The final model for ACE inhibitors controlled for age, race, sex, age and dementia interaction, study site, disease status each year, and ADLs. Dementia onset before CHD did not statistically predict use of ACE inhibitors ($p=0.151$). More limitations of ADLs significantly predicted more use of ACE inhibitors ($p \leq 0.05$; OR=1.00; 95% CI=1.00-1.20) For the categorical variables that measured disease status each year, those who had CHD, but had not yet developed dementia were four times more likely to report taking an ACE inhibitor than those without either disease ($p \leq 0.05$). Participants with both diseases were five times more likely to report taking an ACE inhibitor as compared to those who had not yet developed either disease ($p \leq 0.05$). Post estimation analyses of the categorical variable for timing of disease onset variable shows that among those with CHD only, the use of ACE inhibitors is not significantly different compared to those who have both CHD and dementia. Tables 4.16 present the results for the full model and final model for use of ACE inhibitors for those with dementia before CHD.

Table 4.16: Multivariable results for use of ACE inhibitors for participants who develop dementia before CHD

Variable	ACE Inhibitors					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia before CHD	0.340	1.40	0.36-5.49	0.910	2.48	0.72-8.61
Disease timing variable (no disease)						
CHD only	1.680	5.36	0.69-41.65	1.511*	4.53	0.97-21.06
Dementia only	1.530	4.61	0.89-23.73	1.007	2.73	0.90-8.28
Both diseases	1.861	6.43	0.85-48.64	1.734*	5.66	1.16-27.60
Age (centered)	–0.020	0.95	0.92-1.04	–0.034	0.96	0.91-1.02
Age and dementia interaction	–0.050		0.80-1.12	–0.056	0.94	0.70-1.12
Study site (North Carolina)						
California	0.750	2.11	0.63-7.04	–0.110	0.89	0.28-2.86
Maryland	0.423	1.52	0.59-3.89	–0.107	0.89	0.34-2.32
Pennsylvania	–0.293	0.74	0.21-2.58	–0.817	0.44	0.15-1.29
Race (white)	0.763	2.14	0.70-6.55	0.613	1.84	0.71-4.78
Gender (male)	0.031	1.03	0.47-2.24	0.574	1.77	0.85-3.68
Educational Level (HS or less)	0.365	1.44	0.56-3.66			
Enabling Variables						
Income (≤$24,999)	0.229	1.25	0.48-3.29			
Ever had private insurance	0.557	1.74	0.60-5.05			
Ever had Medicaid	0.245	1.27	0.43-3.78			
Ever had other insurance	0.189	1.20	0.54-2.68			
Ever without insurance	0.434	1.54	0.58-4.10			
Residing in a Nursing Home	0.297	1.34	0.71-2.52			
Care Need Variables						
Activities of daily living	0.066	1.06	0.94-1.20	0.094*	1.00	1.00-1.20
Hypertension	0.030	1.03	0.76-1.37			
Diabetes	0.205	1.22	0.83-1.80			
Renal insufficiency	0.109	1.11	0.49-2.52			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.2.2 Beta-blockers

The full theoretical model for beta-blockers includes 16 independent, control and interaction variables. Two variables (education level and income) would not converge in the model. Table 4.3.2.2 shows all variables included in the full model and the corresponding coefficients, CIs, and ORs. Dementia onset before CHD, the main independent variable, did not significantly predict use of beta-blockers. The categorical variable measuring the timing of disease onset each year predicts use of beta-blockers in the full model indicating that those with both CHD only, even after controlling for all factors, are almost eight times as likely to report taking a beta-blocker compare to those without disease ($p \leq 0.001$) and those with both CH D and dementia are nine times as likely to report using a beta-blocker compared to those without either disease ($p \leq 0.05$). Post estimation analyses of the timing of disease onset control variable shows that among those with CHD only, the use of beta-blockers is not significantly different compared to those who have both CHD and dementia. Other statistically significant predictors in the full model show that those living in a nursing home were 0.33 as likely to report using a beta-blocker ($p \leq 0.01$; OR=0.33; 95% CI=0.18-0.93).

The final model for beta-blockers was developed using the same method described above in section 4.3.2.1. The final predictive model for beta-blockers controlled for age, race, sex, age and dementia interaction, study site, disease status each year, ADLs, and hypertension. Results from the final model show that those who develop dementia before they develop CHD are 0.25 as less likely to report taking a beta-blocker than those who develop dementia after CHD ($p \leq 0.001$; OR=0.25; 95% CI=0.07-0.89). Table 4.17 presents the coefficients, CI, and ORs for the full theoretical and final predictive model for beta-blocker use.

Table 4.17: Multivariable results for use of beta-blockers for participants who develop dementia before CHD

Variable	Beta-blockers					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia before CHD	-1.171	0.31	0.09-1.00	–1.372*	0.25	0.07-0.89
Disease timing variable						
CHD only	2.072**	7.94	1.81-35.10	2.154*	8.62	1.48-50.06
Dementia only	0.806	2.623	0.67-10.34	1.011	3.03	0.61-14.95
Both diseases	2.214*	9.15	1.67-56.11	2.230*	9.31	1.26-68.49
Age centered on mean	–0.033	0.96	0.88-1.03	–0.036	0.964	0.89-1.04
Age and dementia interaction	0.052	1.05	0.96-1.18	0.054	1.05	0.94-1.17
Study site (North Carolina)						
California	0.701	2.01	0.41-9374	0.883	2.42	0.42-13.82
Maryland	0.138	1.14	0.25-5.19	0.305	1.35	0.24-7.48
Pennsylvania	0.744	2.10	0.45-9.89	1.121	3.07	0.61-15.43
Race (white)	–0.189	0.82	0.19-2.59	0.026	1.03	0.27-3.86
Gender (male)	–0.179	0.83	0.26-2.34	–0.418	0.66	0.21-2.01
Education (HS or less) [a]						
Enabling Variables						
Income (≤$24,999)[a]						
Ever had private insurance	0.272	1.31	0.67-6.02			
Ever had Medicaid	–1.162	0.31	0.10-1.04			
Ever had other insurance	–0.527	0.59	0.20-1.71			
Ever without insurance	–0.496	0.60	0.23-1.60			
Residing in a Nursing Home	–1.085**	0.33	0.18-0.93			
Care Need Variables						
Activities of daily living	0.085	1.08	0.90-1.31	0.080	1.08	0.91-1.28
Hypertension	0.102	1.10	0.95-1.25	0.112	1.11	0.98-1.27
Diabetes	–0.010	0.98	0.78-1.24			
Renal insufficiency	0.347	1.41	0.38-5.26			

[a] Not included in the model because of convergence

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.2.3 Lipid-lowering medications

Results from the full model support the hypothesis that those who develop dementia before CHD are less likely to report taking a lipid-lowering medication ($p \leq 0.001$; OR=0.07; 95% CI=0.01 - 0.42). Other variables that significantly predicated a lower likelihood of use of lipid-lowering medications in the full model include the presence of some other (non-private or non-Medicaid) supplemental insurance ($p \leq 0.01$; OR=0.16; 95% CI 0.04-0.54), living in a nursing home ($p \leq 0.05$; OR=0.34; 95% CI=0.13-0.88), and kidney disease ($p \leq 0.05$; OR=0.17; 95% CI=0.04 -0.80). Control variables that significantly predicted higher use of lipid-lowering medications include the Maryland study site ($p \leq 0.01$; OR=8.34; 95% CI=1.88 -37.06), having private supplemental insurance at some point in the study ($p \leq 0.0001$; OR=39.34; 95% CI=6.07 -254.74), or Medicaid as supplemental insurance at some point in the study ($p \leq 0.00$ 1; OR=8.92; 95% CI=2.47-32.15), or being without any supplemental insurance at some point in the study ($p \leq 0.001$; OR=7.10; 95% CI=2.15-23.4).

In the full model, the categorical variable measuring time of disease onset showed that those with CHD only are three times more likely to report taking a lipid-lowering medication compared to those without CHD and dementia ($p \leq 0.001$). Participants with both CHD and dementia are four times more likely to report using a lipid-lowering medication compared to those with either disease ($p \leq 0.001$). Post estimation analyses of the timing of disease onset control variable shows that among those with only CHD, the use of lipid-lowering medication is not significantly different compared to those who have both CHD and dementia.

For the final predictive model, control variables that had a >10% confounding effect or were $p \leq 0.1$ on the bivariate analyses or were theoretically important (e.g. age) were added into the model one by one. The final model for lipid-lowering medications controlled for disease

statues each year, age, race, sex, age and dementia interaction, study site, and ADLs. Having dementia before CHD significantly predicted less use of lipid-lowering medications ($p \leq 0.01$; OR=0.09; 95% CI=0.19-0.46) as well as non-white race ($p \leq 0.5$; OR=0.26; 95% CI=0.91-0.78). Disease status and the Maryland study site significantly predicted more use of lipid-lowering medications ($p \leq 0.01$). Table 4.18 presents the results for the full theoretical and final predictive model for lipid-lowering medications.

Table 4.18: Multivariable results for use of lipid-lowering medications for participants who develop dementia before CHD

Variable	Lipid-lowering Medications					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia before CHD	–2.616**	0.07	.01-.42	–2.356**	0.09	0.02-0.46
Disease timing variable						
CHD only	1.170***	3.22	1.81-5.73	1.750***	5.75	3.55-9.32
Dementia only	–0.593	0.55	0.02-12.96	–1.005	0.36	0.01-14.19
Both diseases	1.478***	4.38	1.81-10.60	0.296**	3.65	1.62-8.23
Age centered on the mean	0.002	1.00	0.92-1.08	–0.019	0.98	0.91-1.05
Age and dementia interaction	0.165	1.18	0.80-1.72	0.081	1.08	0.74-1.58
Study site (North Carolina)						
California	–0.939	0.39	0.07-2.04	–0.274	0.66	0.27-2.10
Maryland	2.122**	8.34	1.88-37.06	1.715**	5.55	1.70-18.18
Pennsylvania	–0.757	0.46	0.09-2.40	–0.392	0.67	0.23-1.94
Race (white)	–0.067	0.93	0.17-4.86	–1.318*	0.26	0.09-0.78
Gender (male)	–0.650	0.52	0.19-1.44	–0.416	0.66	
Education (HS or less)	0.179	1.19	0.25-5.70			
Enabling Variables						
Income (≤$24,999)	–0.980	0.37	0.06-2.14			
Ever had private insurance	3.672****	39.34	6.07-254.74			
Ever had Medicaid	2.188***	8.92	2.47-32.15			
Ever had other insurance	–1.815**	0.16	0.04-0.54			
Ever without insurance	1.960***	7.10	2.15-23.40			
Residing in Nursing Home	–1.087**	0.33	0.12-0.87			
Care Need Variables						
Activities of daily living	–0.085	0.92	0.66-1.27	–0.192	0.82	0.65-1.04
Hypertension [a]						
Diabetes [a]						
Renal insufficiency	–1.753*	0.17	0.03-0.79			

[a] Not included in the model because of convergence

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.2.4 Antiplatelet medications

The full model testing the effect of dements before CHD on the use of antiplatelet medications controlled for 19 independent, control and interaction variables. The main independent variable, dementia before CHD, did not significantly predict use of antiplatelet medication (p=0.9).

To build the final predictive model, control variables that had a >10% confounding effect or that were $p \leq 0.1$ on the bivariate analyses or were theoretically important (e.g. history of arthritis) were added into the model one by one. The final model controlled for disease status each year, age, race, sex, age and dementia interaction, study site, ADLs, and any form of arthritis was forced into the model. In the final model, the developing dementia before CHD was not a significant predictor of the use of antiplatelet medications. As in the other models, the categorical variable measuring disease status at each year was a significant predictor for more use of antiplatelet medication ($p \leq 0.05$) for each category. Table 4.19 displays the coefficients, CIs and ORs for the full and final model for antiplatelet medications.

Table 4.19: Multivariable results for use of antiplatelet medications for participants who develop dementia before CHD

Variable	Antiplatelet Medications					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia before CHD	–0.206	0.81	0.28-2.29	–0.048	0.95	0.32-2.81
Disease timing variable						
CHD only	1.491**	4.44	1.39-14.11	1.646**	5.18	1.54-17.36
Dementia only	1.152*	3.16	1.07-9.36	1.071	2.92	0.93-9.09
Both diseases	1.699**	5.47	1.78-16.74	1.872***	6.50	2.05-20.61
Age centered on the mean	–0.000	1.00	0.95-1.05	–0.009	0.99	0.94-1.04
Age and dementia interaction	–0.033	0.97	0.83-1.11	0.011	1.01	0.87-1.16
Study site (North Carolina)						
California	–0.540	0.58	0.29-1.15	0.080	1.08	0.48-2.43
Maryland	–0.613	0.54	0.25-1.13	0.030	1.03	0.44-2.37
Pennsylvania	–0.352	0.70	0.31-1.58	0.321	1.37	0.58-3.23
Race (white)	1.233**	3.43	1.37-8.59	0.746*	2.10	0.99-4.45
Gender (male)	0.760**	2.14	1.23-3.71	0.330	1.39	0.78-2.45
Education (HS or less)	–0.862**	0.42	0.21-0.82			
Enabling Variables						
Income (≤$24,999)	–0.330	0.71	0.34-1.53			
Ever had private insurance	0.012	1.01	0.50-2.05			
Ever had Medicaid	0.569	1.76	0.80-3.92			
Ever had other insurance	0.003	1.00	0.53-1.89			
Ever without insurance	0.474	1.60	0.70-3.64			
Residing in Nursing home	0.329	1.33	0.11-15.67			
Care Need Variables						
Activities of daily living	0.033	1.03	0.86-1.24	0.011	1.01	0.84-1.20
Hypertension	–0.002**	1.00	0.81-1.21			
Diabetes	0.222	1.24	0.87-1.78			
Renal insufficiency	0.070	1.07	0.46-2.47			
Any arthritis	0.158	1.17	0.71-1.93	–0.043	0.95	0.66-1.38

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.2.5 Compliance with medications

In addition to the four sub-classes of guideline recommended chemoprophylaxis for CHD, two dependent variables that measure compliance with chemoprophylaxis were tested. Participants with CHD who did not report taking any of the four medications were labeled as 0% compliant. Inversely, those with CHD who report taking two, three or all four of the medications are considered 50-100% compliant with guideline-recommended chemoprophylaxis. Similar to the antiplatelet model, 19 variables were tested. The main independent variable, dementia before CHD, did not significantly predict compliance at 0% (p=0.1) or at 50%-100% compliance (p=0.7)

The final models for compliance controlled for disease status each year, age, race, sex, age and dementia interaction, study site, ADLs, and history of hypertension. Having dementia before CHD did not significantly predict compliance. Control variables that significantly predict non-compliance at 0% compliance include race as well as the categorical control variable that measures disease status each year. Results show that whites are less likely to 0% compliant ($p\leq0.01$; OR=0.32 95% CI 0.15-0.68) as are those in all three disease states ($p\leq0.01$).

Having dementia before CHD does not significantly predict compliance at the 50%-100% rate, but the results indicate that those who have CHD only, dementia only, and both disease are more likely to be 50-100% as compared to those without either disease ($p\leq0.01$). Post estimation analyses show that these three states of disease status are statistically different from each other with regard to compliance. Table 4.20 presents the results for the 0% compliance dependent variable models and Table 4.21 for 50-100% compliance for the full theoretical model and final model.

Table 4.20: Multivariable results for 0% compliance with chemoprophylaxis for participants who develop dementia before CHD

Variable	0% Compliance					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia before CHD	0.790	2.20	0.85-5.64	0.253	1.28	0.50-3.28
Disease timing variable						
CHD only	–2.191***	0.11	0.03-0.35	–2.453***	0.08	0.03-0.21
Dementia only	–1.720***	0.12	0.07-0.45	–1.358**	0.25	0.09-0.71
Both diseases	–2.200***	0.11	0.04-0.33	–2.387***	0.09	0.03-0.23
Age centered on the mean	0.006	1.00	0.99-1.07	0.022	1.02	0.97-1.10
Age and dementia interaction	0.114	1.12	0.96-1.30	0.021	1.02	0.88-1.17
Study site (North Carolina)						
California	–0.165	0.84	0.33-2.15	–0.413	0.66	0.30-1.43
Maryland	0.131	1.14	0.49-2.62	–0.106	0.90	0.40-1.99
Pennsylvania	0.163	1.17	0.51-2.76	–0.118	0.89	0.35-2.24
Race (white)	–1.520***	0.22	0.08-0.54	–1.138**	0.32	0.15-0.68
Gender (male)	–0.324	0.72	0.39-1.33	–0.250	0.77	0.41-1.44
Education (HS or less)	0.262	1.30	0.63-2.66			
Enabling Variables						
Income (≤$24,999)	–0.014	0.98	0.45-2.28			
Ever had private insurance	–0.263	0.77	0.34-1.67			
Ever had Medicaid	–0.704	0.50	0.22-1.10			
Ever had other insurance	0.300	1.34	0.66-2.72			
Ever without insurance	–0.684	0.50	0.21-1.19			
Residing in Nursing home	0.360	1.43	.06-35.30			
Care Need Variables						
Activities of daily living	–0.211	0.81	0.64-1.02	–0.189	0.82	0.67-1.00
Hypertension	–0.263*	0.77	0.60-0.99	–0.205	0.81	0.64-1.01
Diabetes	–0.037	0.96	0.64-1.45			
Renal insufficiency	0.105	1.11	0.43-2.90			
Any arthritis	–0.195	0.82	0.43-1.54			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

Table 4.21: Multivariable results for 50%-100% compliance with chemoprophylaxis for participants who develop dementia before CHD

Variable	50-100% Compliance					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
Dementia before CHD	–0.234	0.79	0.22-2.75	–0.326	0.72	0.16-3.21
Disease timing variable						
CHD only	3.183***	24.12	5.71-101.90	2.642***	14.05	4.27-46.20
Dementia only	2.466***	11.77	2.65-52.33	2.129***	8.41	2.66-26.57
Both diseases	3.251***	25.82	5.28-126.25	2.593***	13.3	3.94-45.34
Age centered on the mean	–0.051	0.95	0.88-1.02	–0.019	0.98	0.92-1.04
Age and dementia interaction	–0.060	0.94	0.79-1.12	0.058	1.06	0.88-1.26
Study site (North Carolina)						
California	–0.433	0.64	0.24-1.72	0.791	2.21	0.65-7.43
Maryland	0.192	1.21	0.43-3.37	0.532	1.70	0.58-4.96
Pennsylvania	–0.229	0.80	0.21-2.94	0.580	1.78	0.54-5.90
Race (white)	0.621	1.86	0.45-7.58	0.943	2.57	0.84-7.79
Gender (male)	0.339	1.40	0.68-2.87	0.151	1.16	0.53-2.55
Education (HS or less)	–0.407	0.66	0.26-1.68			
Enabling Variables						
Income (≤$24,999)	–0.231	0.73	0.3431-1.71			
Ever had private insurance	0.995*	2.70	1.04-7.01			
Ever had Medicaid	0.065	1.06	0.34-3.31			
Ever had other insurance	–0.593	0.55	0.26-1.18			
Ever without insurance	0.661	1.93	0.75-4.90			
Residing in Nursing home	0.494	1.63	0.33-8.02			
Care Need Variables						
Activities of daily living	0.042	1.04	0.88-1.23	0.050	1.05	0.87-1.26
Hypertension	0.080	1.08	0.84-1.39	0.095	1.10	0.91-1.33
Diabetes	0.311	1.36	0.97-1.91			
Renal insufficiency	–0.153	0.86	0.127-2.62			
Any arthritis	0.415	1.51	0.94-2.43			

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001

4.3.2.6 Alternative specifications of main independent variable aim 2

The primary independent variable for aim 2 was measured as a static binary variable indicting if the onset of dementia occurred before the onset of CHD (yes or no). The sub-sample for analysis in aim 2 included those who developed both CHD and dementia by the end of the study period, but given that time of development varied, a time-varying categorical variable that captured disease status in each year was included as a control variable. Alternative forms of measuring dementia status were also tested. Sensitivity analyses for aim 2 tested alternative specifications for the dementia status independent variable. They include: the time-varying variable categorical variable alone in the model and a continuous of the number of years with the dementia diagnosis. Each alternative specification was tested with the full theoretical and final models. Table 4.22 presents the results of the alternative specifications of dementia for each model. Odds ratios and 95% confidence intervals for these models can be found in Appendix G. It is important to note that findings on strength of association for predicting use of chemoprophylaxis did not vary between the alternative specifications and the primary measure of dementia status for aim 2.

Table 4.22: Multivariable results of alternative specifications of independent variable for aim 2

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid – lowering Medications	Antiplatelet Medications	0% Compliance	50-100% Compliance
Full model						
Dementia before CHD†	NS	NS	**(negative)	NS	NS	NS
Disease status each year						
No disease (suppressed category)						
CHD only	NS	***(positive)	***(positive)	***(positive)	***(negative)	***(positive)
Dementia only	NS	NS	NS	*(positive)	**(negative)	***(positive)
CHD and dementia	*(positive)	**(positive)	***(positive)	***(positive)	***(negative)	***(positive)
No. of years since dementia diagnosis	NS	NS	NS	NS	NS	NS
Final model						
Dementia before CHD†	NS	*(negative)	**(negative)	NS	NS	NS
Disease status each year						
No disease (suppressed category)						
Has CHD only	NS	***(positive)	***(positive)	***(positive)	***(negative)	***(positive)
Dementia only	NS	NS	NS	**(positive)	**(negative)	***(positive)
CHD and dementia	*(positive)	**(positive)	**(positive)	***(positive)	***(negative)	***(positive)
No. of years since dementia diagnosis	NS	**(negative)	NS	NS	NS	NS

† Primary independent variable

Abbreviations: NS, not significant; CHD, coronary heart disease.

P values: *p≤0.05;**p≤ 0.01;*** p≤ 0.001.

4.3.3 Aim 3

Study aim 3 tests if Medicare beneficiaries who develop CHD *before* dementia more likely to discontinue evidence-based chemoprophylaxis. The analytic sub-sample for aim 3 included only participants who developed CHD *before* dementia and their observations starting with the first year they were on the medication. It was restricted to only those years since to discontinue a medication they must have started in some previous year. Review of the patterns of discontinuation showed that, on average, of those who discontinued a medication 60% discontinued permanently. Multivariable analyses included weighted generalized estimating equations (GEE) models ACE inhibitors, beta-blockers, lipid-lowering medications, and antiplatelet medications. Compliance variables were not included as dependent variables since the goal of aim 3 was to investigate the effect of dementia on discontinuation of each sub-class of chemoprophylaxis.

The main independent variable was the number of years since the onset of dementia. This continuous variable started with "1" in the study year of the diagnosis determined by CHS. All years prior to onset are measured by a "0". Odds ratios (ORs) and accompanying 95% confidence intervals (CI) were calculated to represent the strength of association between use of chemoprophylaxis and the number of years since the onset of dementia.

Construction of the full models varied for each sub-class of medication based on the best theoretical fit of the variable with the medication the model, their significance or confounding characteristics, and limitations on model convergence.

4.3.3.1 ACE inhibitors

Using the logistic GEE models to account for repeated measures, the number of years with dementia did not significantly use of ACE inhibitors (p=.9). Age predicted less use of ACE inhibitors as age and the number of years with dementia increase (p ≤0.01; OR=0.70; 95% CI=0.53-0.92). The California and Maryland study sites (p≤0.05) significantly predicted use of ACE inhibitors as the number of years with dementia increases.

To build the final predictive model to test discontinuation of ACE inhibitors after the diagnosis of dementia, control variables that had a >10% confounding effect or were $p \leq 0.1$ on the bivariate analyses or were theoretically important (e.g. age) were added into the model one by one.

The final model for ACE inhibitors controlled for age, race, sex, study site, and the number of years with CHD. Results do not support the hypothesis that the number of years with dementia would predict less use of ACE inhibitors (p=0.9). Control variables that significantly predicted less use of ACE inhibitors as the number of years with dementia increases include older age ($p \leq 0.05$; OR=0.88; 95% CI=0.78-0.99) and the greater number of years with CHD ($p \leq 0.05$; OR=0.75; 95% CI=0.59-0.96). Control variables that significantly predicted more use as the number of years with dementia increased include the Maryland, California, and Pennsylvania study sites (Compared to the North Carolina site) and being female ($p \leq 0.001$; OR=4.04; 95% CI=1.39-11.7). Table 4.23 presents the results of the full and final models for predicting discontinuation of ACE inhibitors.

Table 4.23: Multivariable results for discontinuation of ACE inhibitors among participants who develop dementia after CHD

Variable	ACE Inhibitors					
	Full Model			Final Model		
Predisposing Variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
No. of years since the dementia diagnosis	–0.033	0.97	0.46-2.01	0.012	1.01	0.62-1.63
Age (centered)	–0.352**	0.70	0.53-0.92	–0.118*	0.88	0.78-0.99
Age and dementia interaction	0.065	1.10	0.98-1.15			
Study site (North Carolina)						
California	4.723*	112.60	2.036-6225.3	2.639**	14.00	1.95-100.00
Maryland	4.080*	59.15	1.88-1859.0	2.587***	13.29	3.26-54.00
Pennsylvania	2.700	14.80	0.31-690.15	1.978*	7.23	1.35- 38.70
Race (white)	–0.807	0.44	0.01-27.04	–1.200	0.30	0.04-2.16
Gender (male)	2.100	8.15	0.92-71.91	1.398**	4.04	1.39-11.7
Educational Level (HS or less)	–0.012	1.00	0.19-5.08			
Enabling Variables						
Income (≤$24,999)	1.322	3.75	0.59-23.70			
Ever had private insurance	1.570	4.80	0.15-150.39			
Ever had Medicaid	–0.773	0.46	0.01-10.89			
Ever had other insurance	2.112*	8.26	0.96-71.13			
Ever without insurance	3.336**	28.12	2.02-391.28			
Residing in a nursing home	0.187	1.20	0.13-11.00			
Care Need Variables						
No. of years since the CHD diagnosis	–0.305	0.73	0.50-1.07	–0.2817*	0.75	0.59-0.96
Hypertension	–0.446	0.64	0.24-1.67			
Diabetes	–0.410	0.66	0.25-1.74			
Renal Insufficiency	–1.200	0.30	0.01-5.15			

Abbreviations: No, number.
[a] Not included in the model because of convergence
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.3.2 Beta-blockers

In the full weighted logistic GEE model, more years with dementia predicts more use of beta-blockers, contrary to the hypothesis of discontinuation.. Race and study site, education, private supplemental insurance and the numbers of years with CHD significantly predict less use as the number of years with dementia increase in the full model.

To build the final predictive model for beta-blockers, control variables that had a >10% confounding effect or were $p \leq 0.1$ on the bivariate analyses or were theoretically important (e.g. age) were added into the model one by one.

The final model for beta-blockers controlled for age, race, sex, study site, age and dementia interaction, the number of years with CHD, and hypertension. Results do not support the hypothesis in that the number of years with dementia did not predict less use of beta-blockers ($p=0.1$). Control variables that significantly predicted less use of beta-blockers as the number of years with dementia increases include the number of years with CHD ($p \leq 0.05$; OR=0.77; 95% CI=0.59-0.99) and the Maryland ($p \leq 0.05$; OR=0.18; 95% CI=0.03-0.91), California ($p \leq 0.05$; OR=0.12; 95% CI 0.02- 0.68), and Pennsylvania ($p \leq 0.05$; OR=0.15; 95% CI=0.02-1.00) study sites ($p \leq 0.05$) (compared to North Carolina). Table 4.24 presents the results of the full and final models for predicting discontinuation of beta-blockers.

Table 4.24: Multivariable results for discontinuation of beta-blockers among participants who develop dementia after CHD

Variable	Beta-blockers					
	Full model			Final Model		
Predisposing variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
No. of years since the dementia diagnosis	0.375**	1.45	1.10-1.92	0.242	1.27	0.92-1.75
Age (centered)	0.086	1.09	0.94-1.25	–0.008	0.99	0.87-1.12
Age and dementia interaction	–0.042	0.95	0.90-1.01	–0.016	0.98	0.93-1.03
Study site (North Carolina)						
California	–2.275*	0.10	0 .01-0.66	–2.090*	0.12	0.02- 0.68
Maryland	–1.614	0.20	0.02-1.58	–1.706*	0.18	0.03-0.91
Pennsylvania	–2.125*	0.12	0.01-0.87	–1.894*	0.15	0.02-1.00
Race (white)	–3.984*	.018	0.01-0.47	–1.492	0.98	0.02-1.90
Gender (male)	1.102	3.01	0.87-10.36	–0.131	0.87	0.31-2.42
Educational level (HS or less)	–1.871*	.153	0.03-0.74			
Enabling variables						
Income (≤$24,999)	–0.003	1.00	0.37-2.63			
Ever had private insurance	1.264*	3.54	1.10-11.32			
Ever had Medicaid	0.481	1.61	0.35-7.417			
Ever had other insurance	–0.237	0.79	0.21-2.90			
Ever without insurance	–0.433	0.65	0.17-2.38			
Residing in a nursing home	–0.694	.499	0.14-1.70			
Care need variables						
No. of years since the CHD diagnosis	–0.420*	0.66	0.45-0.94	–0.260*	0.77	0.59-0.99
Hypertension	0.330	1.39	0.88-2.19	0.019	1.21	0.84-1.74
Diabetes	–0.414	0.66	0.37-1.15			
Renal insufficiency	–0.786	0.45	0.09-2.11			

Abbreviations: No., number.
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.3.3 Lipid-lowering medications

In the full weighted logistic GEE model for lipid-lowering medications, number of years with dementia did not significantly predict use (p=.3). No control variables significantly predicted use of lipid-lowering medications. Level of education, income, and the supplemental insurance status variables did not converge in the model due to the limited number of observations per participant.

Using the same model building method described for ACE inhibitors and beta-blockers, control variables that had a >10% confounding effect or were $p \leq 0.1$ on the bivariate analyses or were theoretically important (e.g. age) were added into the model one by one.

The final model for lipid-lowering medications controlled for age, race, sex, study site, age and dementia interaction, and the number of years with CHD. The main independent variable, number of years with dementia, did not significantly predict use of lipid-lowering medications (p=0.2). Additionally, no control variables that significantly predicted discontinuation of lipid-lowering medications include the greater number of years with CHD. Table 4.25 presents displays the beta coefficients, ORs and 95% CIs for the full and final model of use of lipid-lowering medications for participants who develop dementia after CHD.

Table 4.25: Multivariable results for discontinuation of lipid-lowering medications among participants who develop dementia after CHD

Variable	Lipid-lowering Medications					
	Full Model			Final Model		
Predisposing variables	β coefficient	OR	95% CI	β coefficient	OR	95% CI
No. of years since the dementia diagnosis	–0.747	0.47	0.11-2.038	–0.777	0.45	0.13-1.62
Age (centered)	0.031	1.03	0.74-1.42	0.111	0.89	0.68-1.17
Age and dementia interaction	0.193	1.21	0.86-1.69	0.128	1.13	0.95-1.30
Study site (North Carolina)						
California	–2.647	0.07	0.00-23.59	–2.360	0.09	0.01-16.33
Maryland	–0.757	0.47	0.00-82.1	–1.146	0.32	0.01-51.80
Pennsylvania	–0.658	0.51	0.01-18.80	–2.141	0.12	0.01-11.10
Race (white)	3.268	26.26	0.15-4437.00	3.554	34.96	0.35-3413
Gender (male)	0.625	1.87	0.33-10.43	0.971	2.64	0.42-16.30
Educational level (HS or less)						
Enabling variables						
Income (≤$24,999)						
Ever had private insurance						
Ever had Medicaid						
Ever had other insurance						
Ever without insurance						
Residing in a nursing home	–14.827	3.63	3.59-3.68			
Care need variables						
No. of years since the CHD diagnosis	–0.358	0.70	0.39-1.228	–0.270	0.76	0.55-1.05
Hypertension	–0.358	0.50	0.18-1.381			
Diabetes	–0.700	1.01	0.52-1.956			
Renal insufficiency	–1.606	0.20	00.00-13.16			

Abbreviations: No., number.
[a] Not included in the model because of convergence
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.3.4 Antiplatelet medications

The full model for antiplatelet medications included 17 independent, control and interaction variables. In the full model, the number of years with dementia did not significantly predict discontinuation of antiplatelet medications (p=0.6). The number of years with CHD ($p \leq 0.01$; OR=0.76; 95% CI 0.64-0.90), the California site ($p \leq 0.01$; OR=0.20; 95% CI 0.07 -0.55), and Pennsylvania ($p \leq 0.05$; OR=0.37; 95% CI 0.13-1.00), study sites were significant predictors for less use of antiplaetlet medications as the number of years with dementia increases.

The final predictive model to test the effect of the number of years with dementia on the use of antiplatelet medications controlled for age, race, sex, study site, the number of years with CHD, and a history of any arthritis. The number of years with dementia did not predict discontinuation of antiplatelet medications. (p=0.1). No control variables were significant predictors for use of antiplatelet medications. Table 4.26 presents the results of the full and final models for predicting discontinuation of antiplatelet medications.

Table 4.26: Multivariable results for discontinuation of antiplatelet medications among participants who develop dementia after CHD

Variable	Antiplatelet Medications					
	Full Model			Final Model		
Predisposing Variables	**β coefficient**	**OR**	**95% CI**	**β coefficient**	**OR**	**95% CI**
No. of years since the dementia diagnosis	–0.100	0.90	0.62-1.31	–0.280	0.75	0.54-1.05
Age (centered)	0.004	1.00	0.93-1.07	–0.038	0.96	0.89-1.03
Age and dementia interaction	0.011	1.01	0.97-1.05	0.012	1.10	0.98-1.04
Study site (North Carolina)	–1.585**	0.20	0.07-0.55	–0.196	0.82	0.29-2.27
California	–0.272	0.76	0.28-2.02	0.230	1.24	0.42-3.74
Maryland	–0.981*	0.37	0.13-1.02	0.123	1.13	0.35-3.61
Pennsylvania	0.704	2.02	0.80-5.09	0.550	1.73	0.87-3.46
Race (white)	0.507	1.66	0.88-3.12		1.10	0.55-2.22
Gender (male)	–0.453	0.63	0.34-1.16			
Educational level (HS or less)						
Enabling variables	–0.483	0.61	0.32-1.15			
Income (≤$24,999)	–0.191	0.82	0.28-2.35			
Ever had private insurance	0.205	1.22	0.42-3.54			
Ever had Medicaid	0.212	1.23	0.65-2.32			
Ever had other insurance	0.235	1.23	0.56-2.84			
Ever without insurance	–1.432	0.23	0.03-2.00			
Residing in a nursing home						
Care need variables	–0.270**	0.76	0.65-0.90	–0.035	0.96	0.82-1.12
No. Of years since the CHD diagnosis	0.186	1.20	0.87-1.66			
Hypertension	–0.204	0.81	0.52-1.26			
Diabetes	–0.274	0.76	0.39-1.45			
Renal insufficiency	0.090	1.09	0.62-1.91	0.174	1.19	0.65-2.16

Abbreviations: No., number.
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

4.3.3.5 Alternative specifications of main independent variable aim 3

The sub-sample for the aim 3 analyses are restricted to only participants who developed dementia after CHD. In the main models for aim 3, the independent variable, was measured on a continuous scale based on the number of years a subject had dementia ("0" for every year before onset and "1" starting in the year of onset, then 2, 3…). Alternative forms of measuring dementia status were tested for aim 3 these include: 3MSE score less than 80 and DSST score less than 30. Each alternative specification was tested for the full theoretical model and final model. Table 4.27 presents the results of the alternative specifications of dementia for each model. A graphical display of the odds ratios and 95% confidence intervals for these models can be found in Appendix H.

Table 4.27: Multivariable results for the full and final models testing alternative specifications of dementia status for aim 3

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid -lowering Medications	Antiplatelet Medications
Full model				
No. of years since dementia diagnosis†	NS	**(positive)	NS	NS
3MSE Score Less than 80	NS	NS	NS	NS
DSST Score Less than 30	NS	NS	NS	NS
Final model				
No. of years since dementia diagnosis†	NS	NS	NS	NS
3MSE Score Less than 80	NS	NS	NS	NS
DSST Score Less than 30	NS	NS	NS	NS

† Primary independent variable

Abbreviations: NS, not significant; 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test.

P values: P values: *p≤0.05;**p≤ 0.01;*** p≤ 0.00

5.0 SUMMARY AND DISCUSSION

This dissertation investigates the effect of dementia on whether patients receive guideline-recommended secondary chemoprevention for CHD. Drawing from the literature on predictors of use of health care services and conceptual frameworks regarding physician-related factors for evidence-based medical decision making and patient-level predictors, the analyses compare utilization of chemoprophylaxis for CHD for those with and without dementia. We also examine whether the timing of dementia onset in relation to CHD affects the use of chemoprophylaxis. Although causes for potential variation in use are not empirically tested, the literature reviewed presents theories and data from previous research as to why patients with dementia might be treated differently than those without dementia.

Data from the Cardiovascular Health Study-Cognition Study (CHS-CS) was used to perform a series of sixteen primary analyses that examine differences in the use of chemoprophylaxis for CHD. The main findings are from multivariable analyses focused on different measures of dementia status and on relevant predisposing, enabling, and care need co-variates. Advanced methods were employed to reduce bias and improve the efficiency of the model estimates.

Section 5.1 summarizes the results of the dissertation's three research aims. Section 5.2 discusses and interprets these findings and addresses the limitations. Section 5.3

includes a discussion of the clinical implications from the findings and Section 5.4 discusses the policy implications. Section 5.5 suggests opportunities for future research.

5.1 SUMMARY OF RESULTS

Lipid-lowering medications were the only sub-class of chemoprophylaxis consistently found to be used less among patients with dementia. The following section discusses the general findings on utilization between those with and without dementia and presents the summary of the impact of timing of disease onset on use of chemoprophylaxis.

5.1.1 Effect of dementia on use of guideline-recommended chemoprophylaxis for CHD

Study aim 1 investigated if Medicare beneficiaries with dementia *and* CHD were less likely to report use of evidence-based chemoprophylaxis for CHD compared to those with only CHD. The sub-sample included all participants in the CHS-CS who entered the study with CHD or who developed CHD at some point during the study. For this aim dementia was measured as a binary variable, dementia "yes or no" based on the CHS date of onset. Having dementia does not significantly predict use of use of ACE inhibitors, beta-blockers, or antiplatelet medications. Additionally, dementia was not a significant predictor when compliance when measured as taking none of the four medications (0%) "yes or no".

In contrast, dementia does statistically significant predict less use of lipid-lowering mediations after controlling for age, race, sex, and the interaction between age and dementia and study site. Results indicate that the chances of those with dementia *and* CHD report taking a

lipid-lowering medication are only 38% of the odds of those with CHD only (p<0.05). These findings are consistent with the only other study that has looked at the effect of dementia on the use of lipid-lowering medications (Rodriguez, 2002) that found that among community-dwelling seniors with cognitive impairment, those with dementia were less likely to report taking the medication (OR=0.39, 95% CI=0.16-0.95).

The second finding from our study that supports the hypothesis that dementia has a negative effect on use of chemoprophylaxis is that those with CHD and dementia are only 0.60 times as likely to be 50%-100% compliant with chemoprophylaxis as those with only CHD (p<0.05). Figure 5.1 displays the ORs and 95% CI for each sub-class of chemoprophylaxis and both compliance measures (p≤0.05).

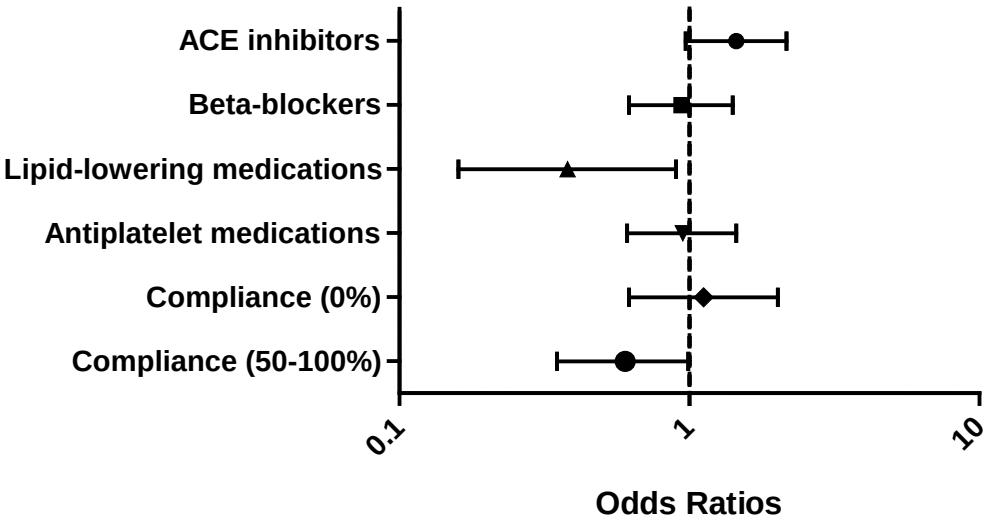


Figure 5.1: Chemoprophylaxis Use Among Participants with CHD and Dementia.

Sensitivity analyses were conducted to investigate if our results depend on the type of dementia. Of the participants who developed both CHD and dementia, 61% developed dementia of the Alzheimer's type, 32% developed vascular dementia and 7% some other form of dementia. The sample was stratified by type of dementia an analyses for aim 1 were repeated for

those with Alzheimer's types and CHD (vs. CHD only) and for those with vascular dementia and CHD (vs. CHD only). Results from the stratified model for Alzheimer's type dementia is consistent with the model for any form of dementia in that it predicts being less likely to be 50%-100% compliance with all four sub-classes of chemoprophylaxis ($p \leq 0.05$). No sub-class of medication, when tested independently, is a significant predictor. Figure 5.2 displays the ORs and 95% CIs for each sub-class of chemoprophylaxis and both compliance measures for those with Alzheimer's type dementia and CHD.

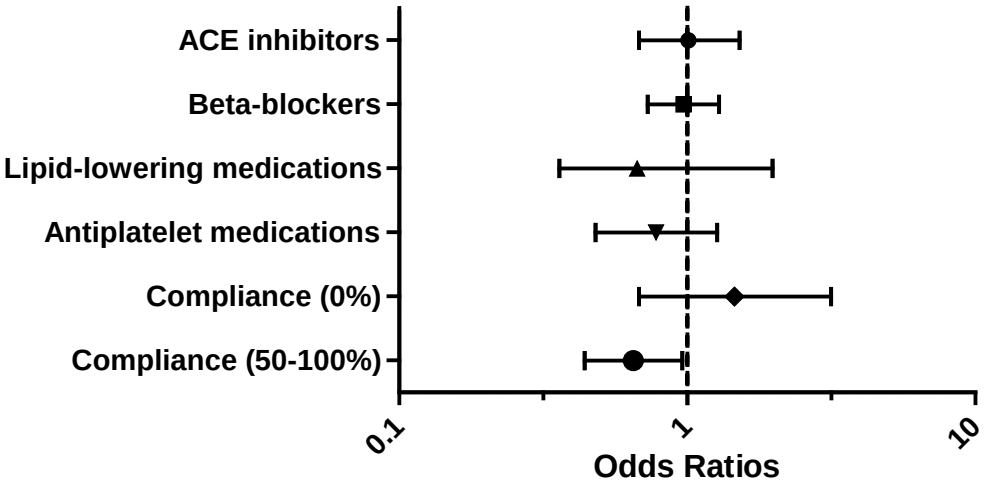


Figure 5.2: Chemoprophylaxis Use Among Participants with CHD and Alzheimer's Disease.

Results from the analysis testing the effect of vascular dementia on the use of chemoprophylaxis were opposite of those from the primary model testing (non-specified) dementia and the model specifying dementia of the Alzheimer's type. Each sub-class of medication is a statistically significant predictor of use. Additionally, those with vascular dementia were less likely to be 0% compliant ($p \leq 0.05$), and more likely to be 50%-100% compliant, although not statistically significant. Participants with vascular dementia were 4.76

times as likely to report using an ACE inhibitor ($p \leq 0.01$; OR=4.76; 95% CI=1.64-13.78) after controlling for age, sex, race, study site, and an age and dementia interaction. In contrast, vascular dementia is a significant predictor for less use of beta-blockers ($p \leq 0.01$; OR=0.48; 95% CI=0.26-0.87), lipid-lowering medications ($p \leq 0.01$; OR=0.46; 95% CI=0.21-0.93), and antiplatelet medication ($p \leq 0.01$; OR=0.38; 95% CI=0.18-0.80). Figure 5.3 displays the ORs and 95% CIs for use of chemoprophylaxis for those with CHD and vascular dementia.

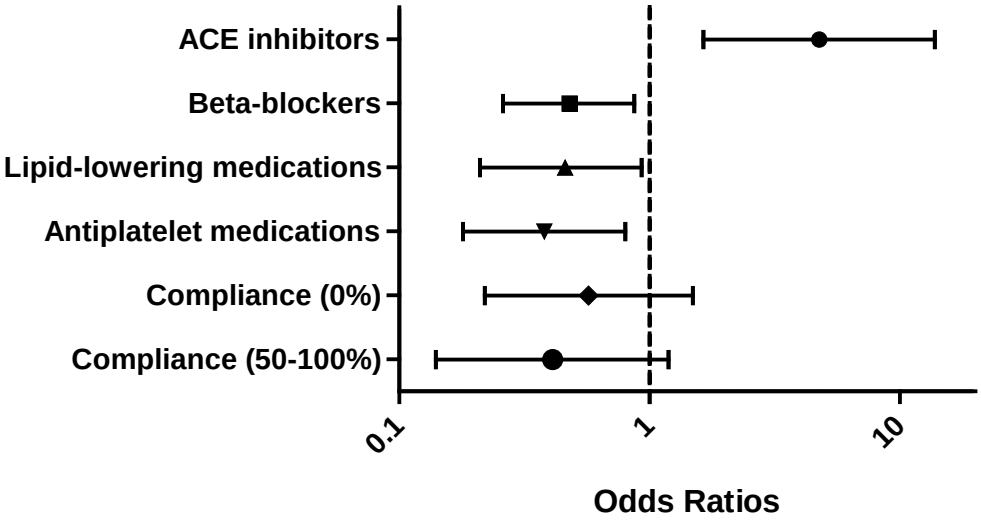


Figure 5.3: Chemoprophylaxis Use Among Participants with CHD and Vascular Dementia.

Results from the analyses testing the effect of vascular dementia on use of chemoprophylaxis show that patient age and the interaction between age and dementia influence use of chemoprophylaxis. Below are predicted probability graphs for each sub-class of medication.

Figure 5.4 shows how the predicted probability of a person with vascular dementia and CHD using an ACE inhibitor changes as their age increases. Use of ACE inhibitors among those with CHD only stays relatively constant over time.

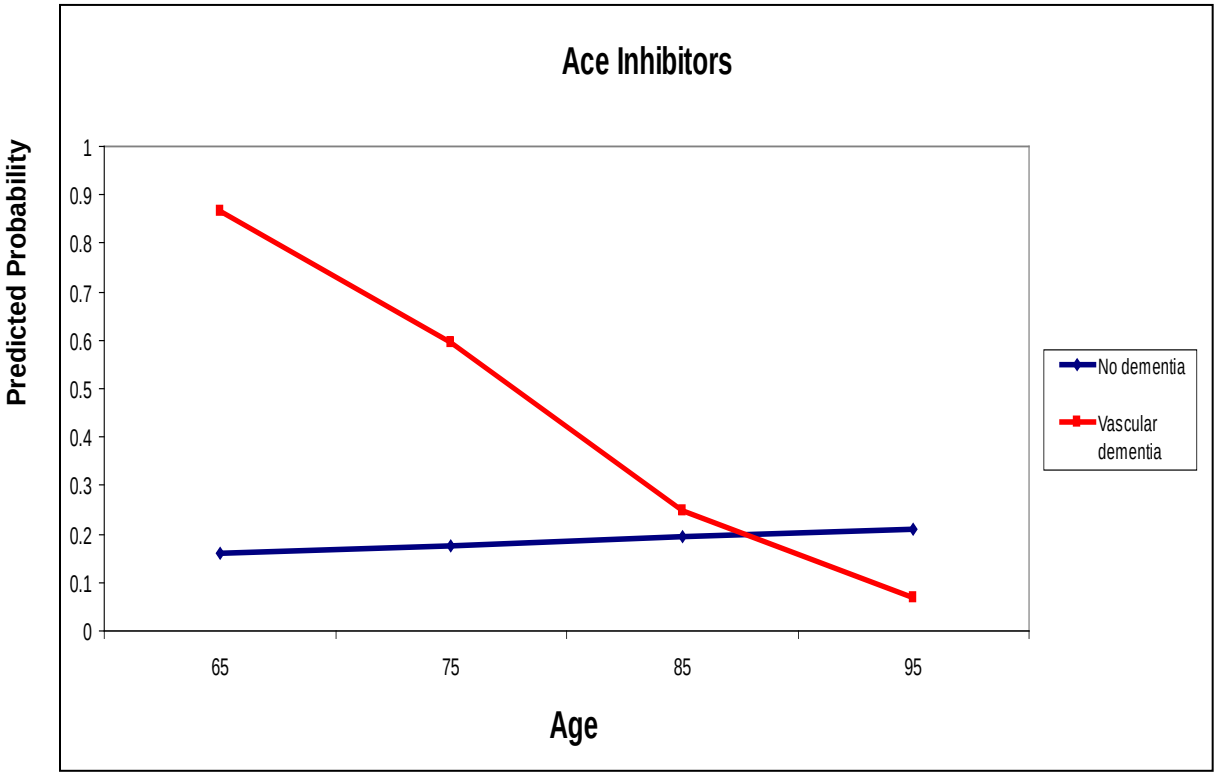


Figure 5.4: Predicted Probability of ACE Inhibitor Use Among those with Vascular Dementia and CHD and CHD Only.

Figure 5.5 shows that the predicted probability of using a beta-blockers increases with age for patients with vascular dementia while those without dementia use of beta-blockers declines.

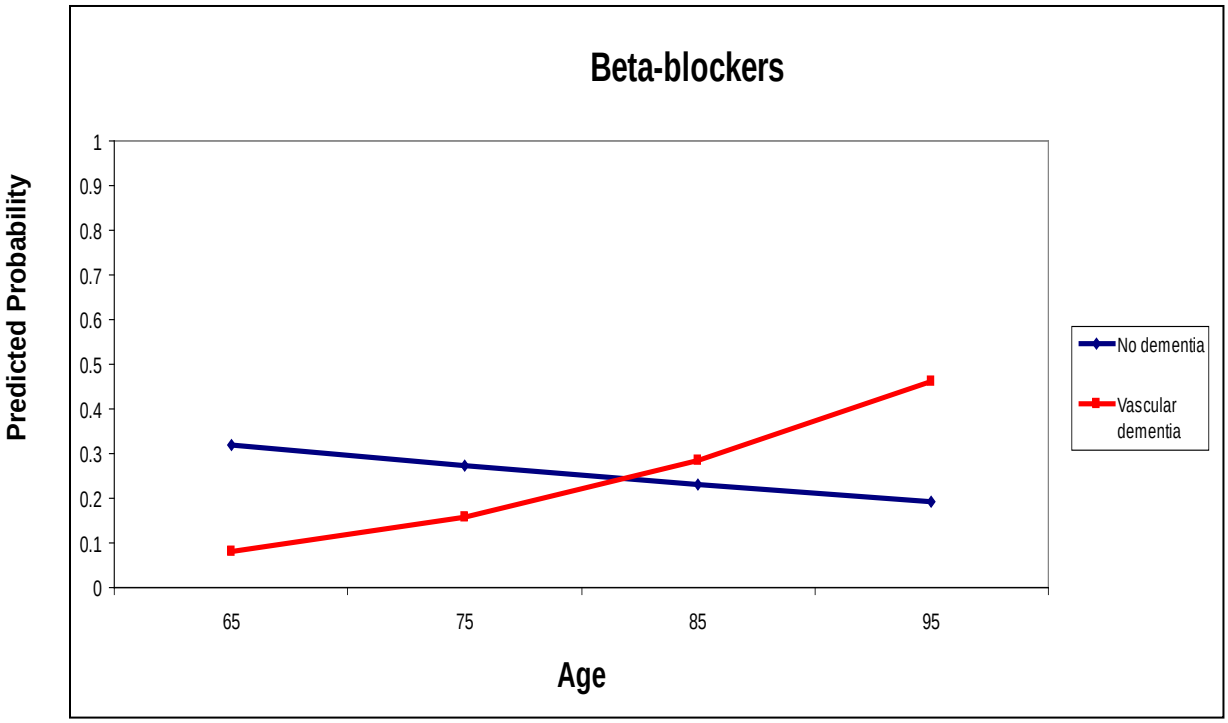


Figure 5.5: Predicted Probability of Beta-blocker Use Among those with Vascular Dementia and CHD and CHD Only.

Figure 5.6 shows the predicted probability of using a lipid-lowering medication for those with and without vascular dementia. The probability of use slightly increases with among those with and without vascular dementia, yet those with vascular dementia have lower probability of use.

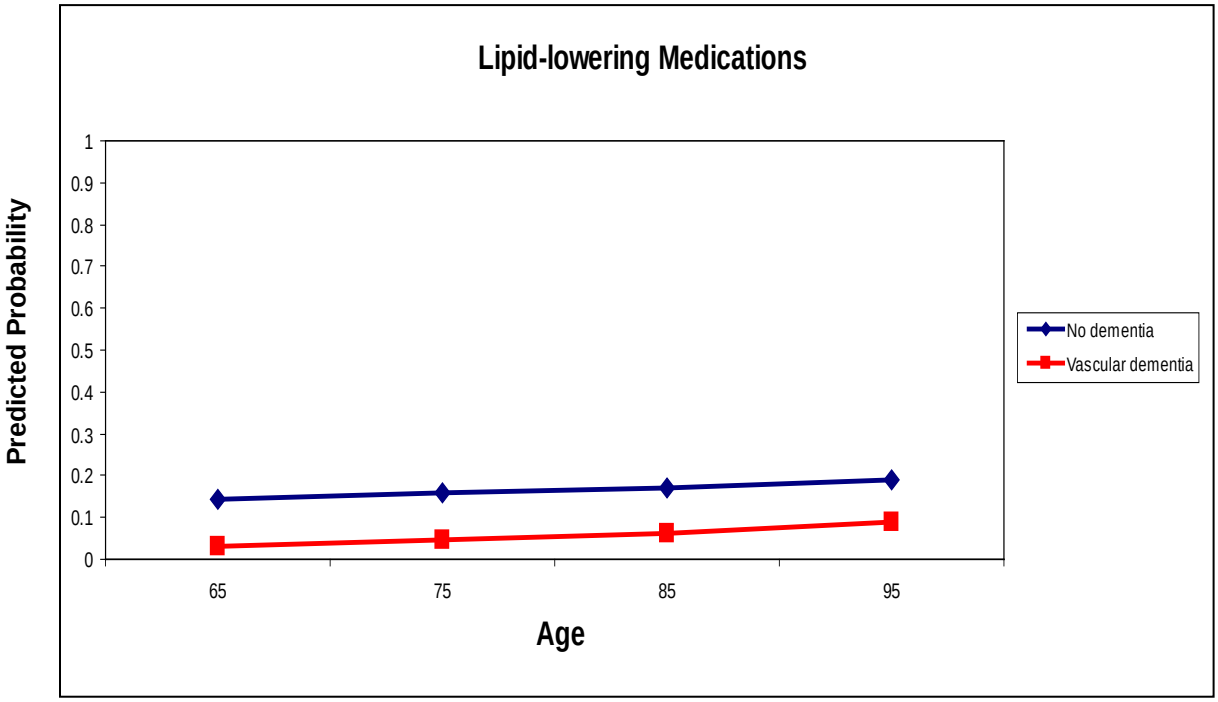


Figure 5.6: Predicted Probability of Use of Lipid-lowering Medications Among those with Vascular Dementia and CHD and CHD.

Figure 5.7 shows that the predicted probability for the use of antiplatelet medications is similar to that for beta-blockers. The probability of using of antiplatelet medication increases more sharply with age for patients with vascular dementia than for patients with only CHD.

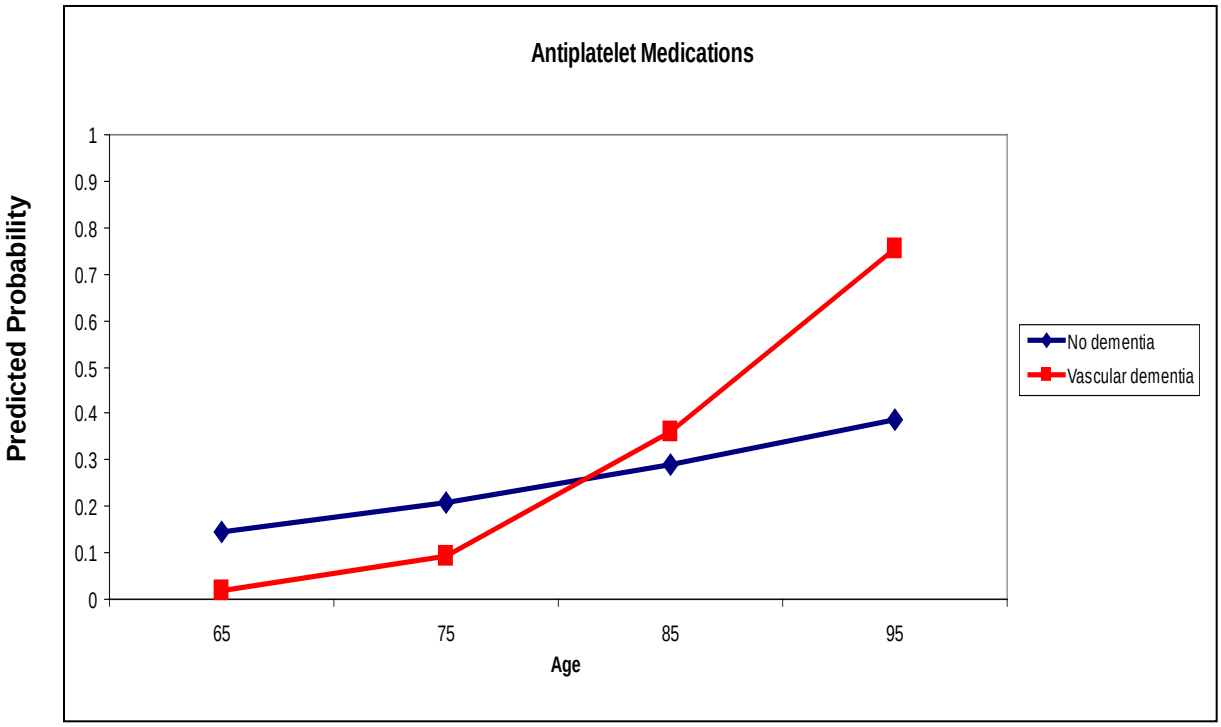


Figure 5.7: Predicted Probability of Use of Antiplatelet Medications Among those with Vascular Dementia and CHD and CHD.

5.1.2 Impact of timing of disease onset

The analyses for aim 2 tested if Medicare beneficiaries who develop dementia *before* CHD are less likely to report use of evidence-based chemoprophylaxis for CHD compared to those who develop dementia *after* CHD. Dementia status was measured as a binary variable of dementia before CHD (yes or no). The results of the analyses show that developing dementia before CHD significantly predicts less use of beta-blockers and lipid-lowering medications. The time of disease onset does not significantly predict the use of ACE inhibitors, antiplatelet medications or compliance with the group of chemoprophlaxis. Based on these findings, and those from the aim 1 analyses, dementia, overall and before CHD, has a negative effect on use of lipid-lowering medications. Figure 5.8 presents the ORs and 95% CIs for use of chemoprophylaxis when the development of dementia precedes the development of CHD.

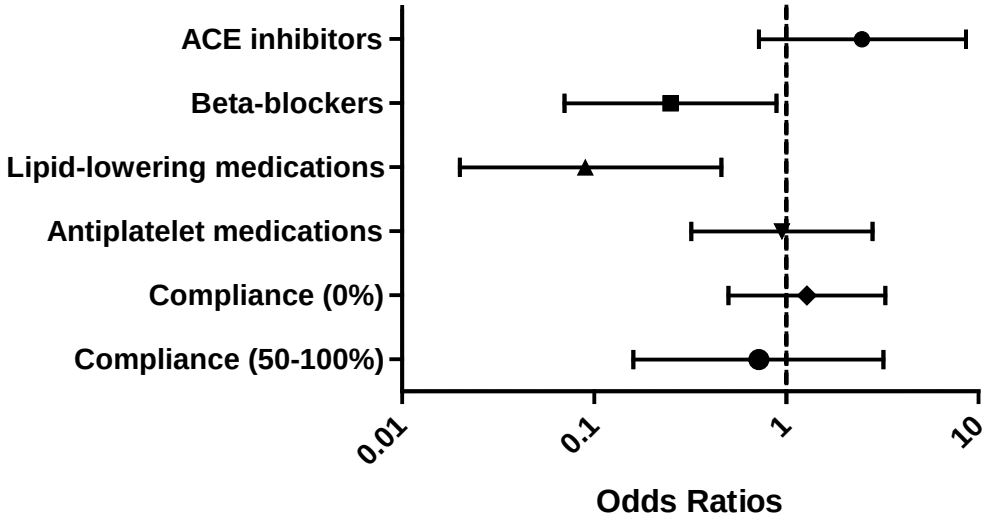


Figure 5.8: Chemoprophylaxis Use Among Participants with Dementia before CHD.

5.1.3 Not starting chemoprophylaxis vs. discontinuing chemoprophylaxis

Results from the analyses for aim 3 indicate that developing dementia after CHD does not significantly predict discontinuation of chemoprophylaxis. Developing dementia *after* CHD was not a significant predictor for discontinuing any type of medication. Figure 5.9 presents the ORs and 95% CIs for use of chemoprophylaxis for those who develop dementia after already starting chemoprophylaxis for CHD.

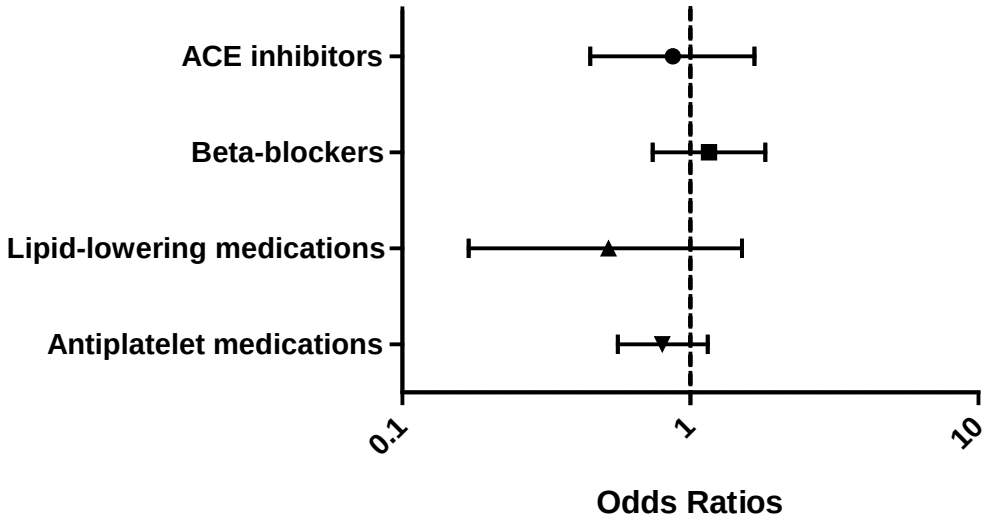


Figure 5.9: Discontinuation of Chemoprophylaxis among Participants with CHD before Dementia.

The absence of discontinuations of chemoprophylaxis after the development of dementia is consistent with what we know from the literature about the infrequency of physicians stopping medications that have already been started (Rhymes, 2000). Traditionally, bioethicists have not made a moral distinction between stopping a treatment versus not starting a treatment if the

outcomes of the action have similar benefits and burdens on the patient. Physicians, on the other hand, do see a distinction between the two (Rhymes, 2000).

Additional social and emotional factors may also affect the difference in rates of not initiating vs. stopping therapy for patients with dementia. For instance, some physicians may not be comfortable initiating discussions about stopping medications as doing so may be seen as a sign of "giving up" on a patient. Additionally, physicians may view advice to patients to stop taking a medication contradicts their advice about the importance of adhering to treatment, especially for secondary prevention of an MI. Despite these pressures, physicians may also overestimate patients' discomfort with stopping medications (Straand, 2001). For patients who are more severely demented and have family participating in medical decision making, the family's inertest in continuing treatment may reflect the need to have a sense of control over a terminal illness by still "actively" treating other comorbidities. The pressure to continue (or initiate) treatment from patients and families may also be a response to the increase in direct-to-consumer advertising for medications (Kravtiz, 2005).

This study, like all others, has limitations that are important to note when considering the implications of the results. Broadly these limitations include measurement of the independent and dependent variable. The dependent variables, use of four sub-classes of chemoprophylaxis, were based on the self-reported use by the study participants. Previous research on medication use among older adults has found that this method of measuring medication often under estimates what physicians are actually prescribing. Findings from the literature also report that, on average, older patients' compliance with prescription medication ranges from 57-70%. Additionally, there is a negative correlation between the number of total prescriptions that a person is prescribed and compliance with any of them (Cline, 1999; Claessens, 1999).

Compliance with medications may be especially challenging for patients with dementia and CHD because of the high number of medications they take and other factors that influence compliance, such as memory, cognitive capacity, executive function and access to getting prescriptions filled (Murray, 2004). Based on previous findings, use of chemoprophylaxis modeled in this study is likely lower than the actual rate of prescribed chemoprophylaxis for patients with CHD and for those with CHD and dementia.

The second limitation includes the measurement of the main independent variable, dementia status. Measures of dementia for this study were based on detailed diagnostic data with an expert committee designated to clinically adjudicate all dementia diagnoses. As noted above, the outcome of interest, use of chemoprophylaxis, was based on participant self-report and not what they were prescribed by their community physician. Based on the data from previous research about physicians' level of awareness of their patient's cognitive status, it likely that a majority of the physicians prescribing the chemoprophylaxis were unaware of what that status was. Data suggests as many as 30-50% of patients have their impaired cognitive status unrecognized by their community physician, therefore the status would have no effect on how physicians' treat non-dementia illnesses. While the design of the study may mirror clinical reality, findings about the effect of dementia on use of evidence-based chemoprophylaxis may be affected by the lack of awareness of cognitive status.

5.2 DISCUSSION

Among the CHS-CS sample of community-dwelling Medicare beneficiaries, we anticipated finding that those with dementia and CHD would consistently be less likely to report using chemoprophylaxis. Additionally, we hypothesized that among the sample with both diseases, the timing of disease onset would impact use and that those who developed dementia first would have lower rates compared to those who developed CHD first. Additionally, we believed that among those who developed CHD first, use of chemoprophylaxis would decline due to discontinuation once the person developed dementia. The hypotheses were based on a number of findings from the literature about possible factors that may lead to less aggressive care for patients with dementia compared to their peers without dementia.

Our findings show that for lipid-lowering medications there was lower use across aims 1 and 2. Also, the findings regarding the group with vascular dementia may provide the most interesting results in that CHD is a known risk factor for developing vascular dementia, yet use for all sub-classes, with the exception of ACE inhibitors, is lower overall and is highly related to patient age. Our hypotheses were based on three beliefs for why those with dementia may be treated less aggressively. First are the unique features of dementia on both physical and cognitive abilities and its impact on life expectancy, second, the imposition of physician value judgments about the quality of life of a person with dementia, and third, the impact of less aggressive patient and family goals for care on the choices for treatment. Our findings from the empirical analyses do not provide causal evidence, they support the overall theory that the presence of dementia, comorbid with CHD, may result in less use of some types of chemoprophylaxis as well as overall compliance with chemoprophylaxis.

First, we anticipated finding different rates of utilization of chemoprophylaxis because of clinical factors that make dementia an unusually complex disease. These include the interaction of cognitive and functional symptoms that overtime decrease life expectancy and quality of life (Boustani, 2003; Fried, 2002). When physicians make treatment decisions for patients with CHD and dementia, medically relevant factors, such as life expectancy, the inability to adhere to treatment recommendations, and the increased risk of harm from a treatment impact their decisions and, we believe, decrease the likelihood of them recommending evidence-based chemoprophylaxis (Brauner, 2000; Monette, 1997). For example, a physician might consider that the patient's life expectancy is less than the expected benefit from a particular treatment. Also, that a patient's cognitive disabilities and memory problems could result in them not following the correct prescribing recommendations, hence putting them at high risk of adverse events. An example may be the risk of a fall for someone taking an antiplatelet medication, such as a subdural hematoma, which may render the patient with dementia in a worse state (Karnath, 2004). Another example is that the number of competing biomedical, functional, and behavioral issues that the dementia patient may be experiencing "pushes" the treatment of CHD to a lower priority for the physician, as well as for the patient, or family (Silverman, 1997).

The second belief that shaped our hypotheses of lower use of chemoprophylaxis is the effect of dementia on the progressive loss of cognitive abilities. Dementia erodes the characteristics that define us as human, such as memory, personality, and awareness of self and others. These manifestations of the disease make patients with dementia vulnerable to negative perceptions and judgments about their quality of life and social worth. The judgments are likely to impact physician decision-making. We know from the literature that patients' cognitive abilities and sociological features may negatively influence treatment (Crane, 1975; Eisenberg,

1979; Marwill, 1996). The imposition of value judgments on the decision-making process, without any input from the patient, could affect what evidence about the optimal treatment is analyzed and how information about those treatments is presented to patients and families.

The third reason we believed that patients with dementia would have lower rates of some sub-classes of guideline-recommended chemoprophylaxis is that the patients' prefer less aggressive care. If this preference is communicated to the physician, it may impact treatment and result in lower rates of utilization. We recognize that the literature on the impact of patient preferences on treatment outcomes is inconsistent, at best, and that it assumes that physician, patients, and families have had some discussion about goals of care. Nonetheless, it is an important factor to consider given that dementia is a terminal disease and that patient compliance with chemoprophylaxis requires that they take an active role (i.e. filling prescriptions and taking the medications). The literature on the effect of patient preferences on receipt of intense hospital-based treatment at the end-of-life shows that patient preferences tend to have little impact on the treatments that patients' actually receive (Teno, 1997). In contrast, some studies have shown that less aggressive goals of care that are discussed between the physician and patient result in lower rates of out-patient planned care such as primary preventive procedures (Flood, 2006). Although no studies have looked at the effect of patient preferences on the use of chemoprophylaxis for CHD, we believe that for patients with dementia, patient preferences may have an effect on utilization for two reasons. The first is based on the idea stated above, that dementia is a terminal disease, with a progressive decline, that many believe leads to a life with little quality. Because of this, physicians, patients and families may be more open to talking about preferences and actively incorporating them into treatment plans for other conditions. Second, compliance with chemoprophylaxis requires that patients take an active role and, if the

intended or anticipated outcomes of the use of chemoprophylaxis (i.e. reduce the risk of mortality from an MI) are not aligned with patient goals, physicians may be less inclined to be compliant with evidence-based guidelines. Physicians and families may believe that treating the CHD may only prolong their existence with dementia and rob them of the benefit of dying sooner and more suddenly from an MI rather than decline over a period of years with dementia.

5.2.1 Lack of variation in use of chemoprophylaxis

We hypothesized lower rates of utilization of chemoprophylaxis for patients with dementia and CHD. Our findings for lipid-lowering medications and 50-100% compliance with all sub-classes support this hypothesis, as do the findings on the effect of vascular dementia on utilization. But, the remainder of the findings for the other sub-classes from this study are predominantly negative. For example, dementia does not appear to negatively impact the use of ACE inhibitors. We believe there are three primary explanations for the negative findings. The first is the lack of knowledge of the prescribing physician about a patient's cognitive status. Second is the medical uncertainty that dementia may add to the decision-making process for treating comorbidites, and third is the low level of burden and risk that chemoprophylaxis for CHD pose to patients.

It has been documented in the literature that primary care physicians' awareness of a patient's cognitive status is often not accurate, especially in the earlier stages of dementia (Chodosh, 2004; Valcour, 2000). It has been estimated that nearly 35% of patients with dementia have their disease go unrecognized or undiagnosed by their primary care physician (Valcour, 2000). As a result, physicians may treat patients with CHD and dementia the same as those without dementia and not question providing guideline-recommended treatment. No data exists

on the level of cardiology sub-specialists' awareness of cognitive status when making treatment decisions for older adults with CHD.

In this study, the main independent variable, dementia status, has a clinically adjudicated date of dementia onset based on neuroimaging (MRI), multiple cognitive measures, and medical record review by trained neurologists (Lopez, 2003). This level of diagnostic testing for dementia is uncommon in the community, even for patients who complain of memory loss and present to their primary care physician with signs of dementia (Bounstani, 2003). The main dependent variables for this study are four sub-classes of cardiovascular medications that are reported as being used by the participants, but presumably prescribed by a provider in the community who did not have access to the detailed cognitive status information collected by CHS. Data on the community physicians' knowledge of the study participants' cognitive status was not collected by the CHS. Based on these two measures, and what we know from the literature, it is possible that the physician's who recommended or prescribed chemoprophylaxis were not aware the patient's dementia status (Lopez, 2008). If the lack of variation in chemoprophylaxis is an accurate representation of what occurs in practice, it may explain variation in treatment for patients with CHD and dementia in the community, such as those observed by Hanlon (1996).

The second possible reason for the lack of variation in chemoprophylaxis may be the medical uncertainty and complexity that a patient's cognitive impairment adds to the medical-decision making process. For example, the presence of dementia can affect the patient's ability to give an accurate medical history (Adams, 2005) and to report symptoms and adverse events from medications (Brauner, 2000). The literature on variation has demonstrated that physician uncertainty often leads to more conservative treatment, more testing and increased use of

diagnostic procedures (Eddy, 1984). For patients with dementia and CHD, therapeutic caution may cause physicians to pay more attention to clinical practice guidelines and more likely to follow evidence-based recommendations (Adams, 2005).

The third reason for finding similar use of chemoprophylaxis may be the low initial burden and long-term burden of taking chemoprophylaxis for CHD. Medical and surgical health care services include a range of interventions from primary preventive screening and diagnostics to intensive, life-sustaining treatments. All interventions involve some risk and burden on the patient, but the medical community demands that there be a reasonable expectation of benefits and the magnitude of the benefits should be commensurate with the probability and degree of risk (Brock, 1995). Use of chemoprophylaxis (1) is proven to reduce mortality from MI, but require ongoing use for the patient to continue to receive benefit; (2) is low-burden, oral medications with few side-effects and a low probability of adverse events; and (3) is relatively inexpensive. Secondary chemoprophylaxis is different from other treatments, in that the assumption, based on the evidence, is that strict adherence with chemoprophylaxis may reduce the risk of a subsequent MI, although the exact reduction in risk is not known. It is assumes that the risk of a subsequent MI is increased if the patient does not take chemoprophylaxis, but that exact rate is also unknown. In between each of these extremes are an array of possible outcomes, many of which we do not know exact information on their chance of occurring and are very difficult to align with patients goals of care.

The array of outcomes of treating (or not treating) CHD and aligning those outcomes with patient goals is different and much more difficult than deciding whether to conduct primary screening. For example, a decision not tp perform a mammogram on a patient who would not consider any treatment even if a cancer was detected is easily justified because does not align

with the screening benefit or the patient's goals. Unless a patient has clear and explicit goals that they want to discontinue all treatments in the hope of dying sooner from something other than dementia, it is more difficult to align use with patient goals.

Chemoprophylaxis for CHD also differs from intensive, life-sustaining interventions that must be continued indefinitely for the patient to receive continued benefit. Such interventions include long-term ventilatory support or hemodialysis. The burden of these treatments is high and the impact on quality of life is greater (Rhymes, 2000). These treatments often pose substantial risks, but without the treatment the patient will die either immediately or shortly after withdrawing the treatment (or after not initiating treatment.) In the studies by Marwill (1996) and Sloan (2004), patients with dementia had lower rates of surgical resection for breast cancer and catheterization, coronary angioplasty, and cardiac bypass surgery for CHD. In each of these studies the intervention was surgical, burdensome and put the patient at risk of complications and iatrongenic events. Neither Sloan nor Marwill investigated casual factors for the lower rates for patients with dementia, but we hypothesize that the parties involved in the decision-making process determined that the benefit gained for the patient, extension of life, did not outweigh the risks of immediate death or complications that could decrease the quality of the remaining years of life.

5.3 CLINICAL IMPLICATIONS

As people age the incidence of morbidities from life-limiting illnesses increases and as these illnesses progress it is not uncommon that people's goals of care shift from curative to disease-modifying to the management of symptoms (Fox, 1997). We believe that reevaluating the use of

health services to fit changing goals of care is an essential component of quality care for patients with dementia. To improve care for people with dementia, many medications previously indicated for the treatment of a comorbid condition may need to be altered or even discontinued in order to better align treatments with patient goals, promote quality of life, reduce the burden on the patient and family and reduce the risk of adverse effects (Hajjar 2007). Some studies have shown that people with dementia are at greater risk of receiving overly aggressive care that does not align with their goals of therapy (Mitchell, 2004; Mehta, 2010) and of under treatment of symptoms that could decrease symptom burden and improve quality of life (Frampton, 2003).

The successful alignment of goals of care with the use of chemoprophylaxis is an essential element in the medical decision-making process for patients with CHD and dementia. To implement this in clinical practice requires the consideration and discussion of all likely outcomes for the patient with and without treatment. This includes determining whether a reasonable benefit has already been achieved from the medications the patient has been using and whether any additional benefit is anticipated or desired based on the patient's goals of care (Holmes, 2006). Also a consideration in the decision-making process should be time-until-an adverse event is likely to occur. This occurs when the likelihood of experiencing a risk from the treatment is as likely as achieving a benefit based on the patient's condition.

To determine the time-until-benefit or the likely-time-until-adverse event requires analysis of the evidence. The Eddy framework for evidence-based decision-making includes this important step, but we believe that in making medical decisions for people with dementia, the Eddy model does not account for the array of outcomes that could occur without an intervention and for a variety of different interventions. Our interpretation of the Eddy model assumes that a single problem has been identified and prioritized by the physician and that there is one best

evidence-based solution to “fix it” (Lynn, 1991). This approach is not helpful for making treatment decisions for patients with dementia and CHD given the possibilities of various outcomes of both diseases and their dependence on how or if they are treated. Identifying the array of outcomes of treatment is not always easy and describing them to patients and their families may be more difficult. Nonetheless these steps are critically important for quality care because the treatment chosen is likely to have a substantial impact upon the length and nature of their remaining years. A recent study by Mitchell (2010) suggests that family members of patients with advanced dementia would be far less likely to favor particular treatments, especially those considered high risk and burdensome, if they had a better understanding of dementia as a progressive disease that attacks the body, as well as the mind, and if they understood the implications of the treatments on the progression of dementia.

A medical decision-making framework developed by Holmes (2006) for prescribing medications for patients’ late in life is particularly useful when considering medication management for patients with dementia. The model takes into account whether a patient it likely to benefit from a particular medication by comparing the patient’s estimated remaining life expectancy with the time until the medication benefit is achieved. In addition, the medication must fit into a logical treatment plan as determined by the concordance between the patient’s goals of care and the treatment targets of the medication.

5.4 POLICY IMPLICATIONS

This study has added to the body of previous work by controlling for type of dementia, severity of cognitive status, functional status, and length of time with the dementia and CHD. Unlike

intense, life-sustaining treatments, guideline-recommend chemoprophylaxis is low burden, low risk, and low cost. Yet, they differ from life-sustaining treatments and primary preventive screening in that it is more difficult to predict health outcomes with and without treatment and align those outcomes with patient goals of care.

The data used for this study were collected prior to Medicare Part D and quality improvement initiatives within Medicare that link payment for health services with health outcomes based on the evidence. The introduction of value-based purchasing, such as pay-for-performance (PFP) in health care, has been presented as a model to reform the current payment structure within Medicare. In traditional Medicare, physicians are reimbursed on a fee-for-service model which is based on the number and complexity of services provided, without regard to quality, efficiency, or impact on their patient's health outcomes. Pay-for-performance, and other programs that link health outcomes to payments, are designed to promote the actuation of evidence-based medicine with the goals of improving quality and reducing waste within the system. Clinical practice guidelines for the secondary prevention of CHD were available to physicians during the time that the CHS data were collected, but with the exception of the Veterans Administration Health Care System (Walter, 2001), physicians had no incentive to follow the guidelines. Despite this, our study consistently found similar patterns of use for ACE inhibitors and antiplatelet medications.

The impact of PFP on health services utilization for patients with dementia has not been studied. There is concern that PFP could result in a reduction in quality of care for older patients with comorbidites if the unique needs of this population are not appropriately accounted for in the performance measures. In recent study by Ryan (2010), results from one Medicare PFP Demonstration project did not reduce access to cardiovascular care for older minority patients

who were admitted with an MI. Although the CHS data were collected before PFP, we believe that, if replicated in the present environment rates of use for all sub-classes of chemoprophylaxis would be similar for those with and without dementia, indicating a lack of opportunity or disincentives for physicians to adjust their medical decision-making and treatment recommendations based on the array of outcomes that are appropriate for patients with dementia and CHD.

In 2005, Medicare (combined with Medicaid) spent $112 billion for care of patients with dementia (Alzheimer's Association, 2007). Pay-for-performance programs in Medicare have the potential to improve quality and reduce the cost of health services for people with dementia, but it is essential that measures of performances be based not only on the evidence, but also account for the convergence of possible outcomes of each disease with and without particular treatments. Additionally, PFP programs in Medicare must not unwittingly lead to a decrease in access to care for patients with dementia if their goals of care translate into less aggressive treatment or care plans that deviate from evidence-based care that are not financially rewarded within the Medicare system.

5.5 FUTURE RESEARCH

This study serves as the basis for future work in a number of areas. One area includes research on medical decision-making and the disentanglement of physician, patient and environmental factors on the use of health services for older adults with dementia. This work could provide valuable information for heightening physicians' awareness of their personal influence on the process and provide preliminary information for interventions that improve how physicians

present information about treatment options and outcomes to patients with dementia and other comorbidities.

Based on our findings it is also important that any study designed to identify factors that influence medical decision-making for patients with dementia must address the issue of physician awareness of a patient's cognitive status. For example, a study question may be, does increasing the primary care physician's awareness of a patient's cognitive status affect treatments for non-dementia chronic diseases? Is there an impact on clinical outcomes or mortality or quality of life outcomes?

As described in chapter 2, the guideline-recommended, evidence-based treatments investigated in this research are grounded in a robust evidence base with data about the effectiveness of these medications from multiple clinical trials, yet, none of the trials included patients with dementia. It was assumed for this research that the use of chemoprophylaxis reduces the risk of subsequent MIs in patients with and without dementia at the same level. Research that compares the outcomes of treatments for different groups is needed. The purpose of this type of research is twofold. It would help physicians make informed decisions about the treatment options they offer and discuss with patients. Second, it would help patient and families understand a more realizable benefit of treatment. Research that strengthens the evidence-base and is available to facilitate better health care choices could improve the quality of health care for patients with dementia. An example of such a study would be the effectiveness of the use of pacemakers for sinus node dysfunction among patients with dementia or the effectiveness of warfarin for the secondary prevention of strokes for patients with vascular dementia. This line of research is important to understand the optimal decisions for care of patients with dementia and could produce a more profound understanding of the effectiveness of treatments for patients with

dementia, their impact on quality of life, and the clinical factors that influence medical decision-making for patients with dementia and other comorbidities.

Finally, an area for future research is to investigate the role of families of in the medical decision-making process when the treatment choices have uncertain outcomes that are not easily aligned with the patient's perceived goals. An example of a research question would be do families make explicit decisions about compliance with secondary chemoprophylaxis? Medical decision making for patients' with dementia frequently falls upon the family, with guidance from physicians. Factors such resources available to families and differences in perception of quality of life between clinicians and caregivers may affect decisions (Fitzpatrick, 2004). Advance directives and other documented wishes regarding health services may aid families in decision-making, but they do not adequately represent the family's preference for how the patient should be treated. This is especially true for treatments that have uncertain and varied outcomes that may impact both quantity and quality of life.

APPENDIX A

IRB APPROVAL

University of Pittsburgh

Institutional Review Board

Exempt and Expedited Reviews
Christopher M. Ryan, Ph.D., Vice Chair
3500 Fifth Avenue
Suite 105
Pittsburgh, PA 15213
Phone: 412.383.1480
Fax: 412.383.1146
e-mail: irbexempt@msx.upmc.edu

TO: Nicole Fowler
FROM: Christopher M. Ryan, Ph.D., Vice Chair
DATE: August 27, 2004
PROTOCOL: Treatment Variation in Secondary Preventive Care for Cardiovascular Disease Among Elderly Medicare Patients with Dementia
IRB Number: 0408086 **Approval Date**: August 26, 2004

The above-referenced protocol has been reviewed by the University of Pittsburgh Institutional Review Board. Based on the information provided in the IRB protocol, this project meets all the necessary criteria for an exemption, and is hereby designated as "exempt" under section 45 CFR 46.101(b)(4). The regulations of the University of Pittsburgh IRB require that exempt protocols be rereviewed every three years. If you wish to continue the research after that time, a new application must be submitted.

- If any modifications are made to this project, please submit an 'exempt modification' form to the IRB.
- Please advise the IRB when your project has been completed so that it may be officially terminated in the IRB database.
- This research study may be audited by the University of Pittsburgh Research Conduct and Compliance Office.

APPENDIX B

UNADJUSTED USE OF CHEMOPROPHYLAXIS AMONG PARTICIPANTS WITH CHD STUDY YEARS 2-11, NO. (%)

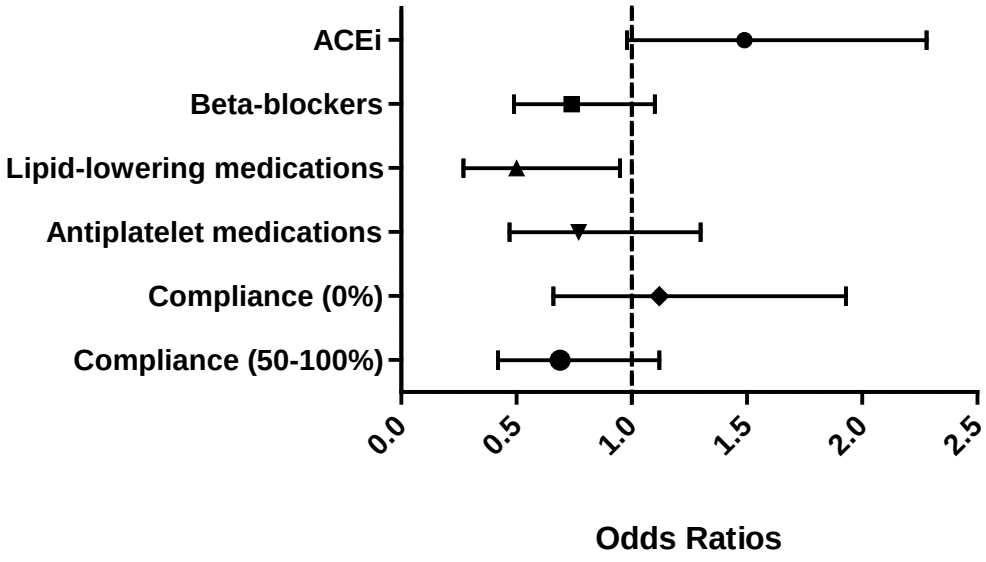
Dependent Variable	Study Year 2	Study Year 3	Study Year 4	Study Year 5	Study Year 6	Study Year 7	Study Year 8	Study Year 9	Study Year 10	Study Year 11
ACE inhibitors	41 (8)	55 (10)	78 (13)	110 (15)	120 (16)	138 (18)	151 (20)	151 (21)	175 (24)	181 (24)
Beta-blockers	153 (30)	159 (29)	161 (27)	185 (26)	197 (26)	207 (27)	203 (27)	213 (29)	239 (32)	256 (35)
Lipid-lowering medications	46 (9)	56 (10)	66 (11)	84 (12)	107 (14)	113 (15)	125 (17)	146 (20)	181 (24)	206 (28)
Antiplatelet medications	286 (56)	327 (60)	376 (63)	445 (62)	457 (62)	475 (63)	455 (62)	419 (59)	443 (62)	445 (65)

Abbreviations: CHS-CS, Cardiovascular Health Study-Cognition Sample; ACE Inhibitors, Angiotensin- Converting Enzyme Inhibitors

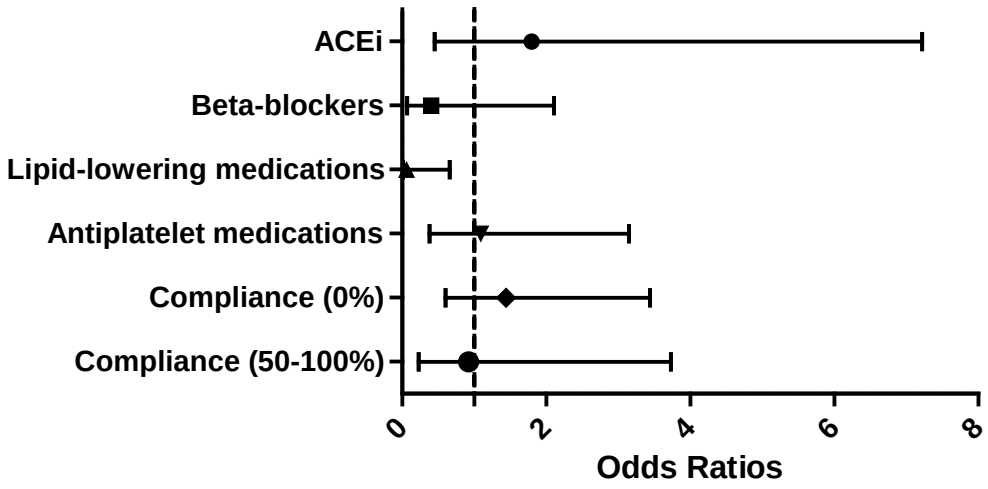
APPENDIX C

ODDS RATIOS AND 95% CIS FOR FINAL PREDICTIVE MODELS USING EXCHANGEABLE CORRELATION STRUCTURE

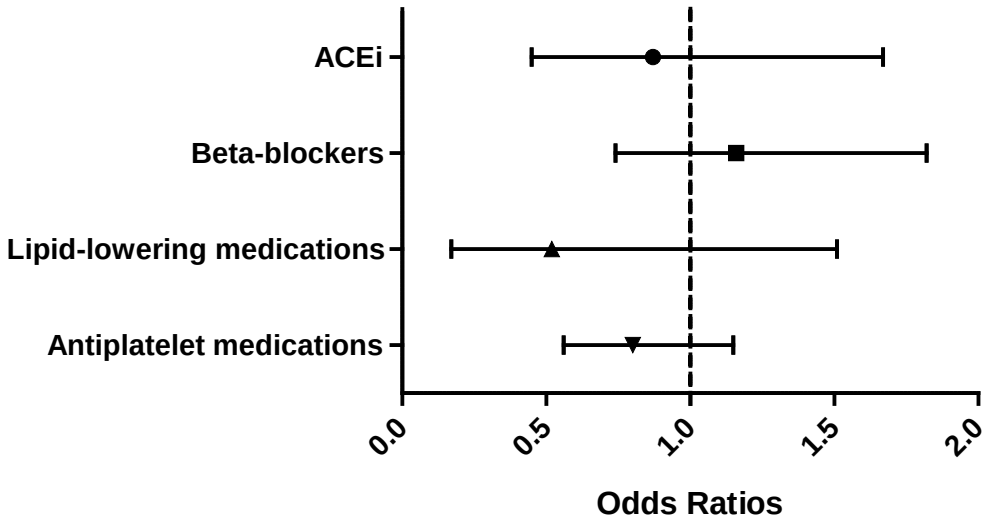
C.1: Odds Ratios and 95% Confidence Intervals for Final Aim 1 model of Chemoprophylaxis use for Participants with Dementia using Exchangeable Correlation Structure



C.2: Odds Ratios and 95% Confidence Intervals for final aim 2 model of Chemoprophylaxis use for Participants with Dementia before CHD using Exchangeable Correlation Structure



C.3: Odds Ratios and 95% Confidence Intervals for final aim 3 model of Chemoprophylaxis use for Participants with Dementia after CHD using Exchangeable Correlation Structure



APPENDIX D

RESULTS OF NON-WEIGHTED BIVARIATE ANALYSES FOR ALL POSSIBLE SPECIFICATIONS OF DEMENTIA STATUS

D.1: Results non-of weighted bivariate analyses for all possible specifications of dementia status for study aim 1

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid-Lowering Medications	Antiplatelet Medications	0% Compliance	50-100% Compliance
Dementia (present in that year)†	*(positive)	NS	NS	NS	*(positive)	NS
Dementia at baseline	NS	**(negative)	*(negative)	**(negative)	***(positive)	***(negative)
Prevalent Dementia	NS	**(negative)	***(negative)	*(negative)	***(positive)	**(negative)
3MSE Score Less than 80	NS	NS	*(negative)	**(negative)	**(positive)	*(negative)
DSST Score Less than 30	***(positive)	NS	NS	***(negative)	**(positive)	NS

† Primary independent variable

Abbreviations: NS, not significant;3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test.

P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

D.2: Results of non-weighted bivariate analyses for all possible specifications of dementia status for study aim 2

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid – lowering Medications	Antiplatelet Medications	0% Compliance	50-100% Compliance
Dementia before CHD †	NS	*(negative)	**(negative)	***(negative)	***(positive)	**(negative)
Disease status each year						
No disease (suppressed category)						
CHD only	**(positive)	***(positive)	**(positive)	***(positive)	***(negative)	***(positive)
Dementia only	NS	NS	NS	NS	NS	NS
Both diseases	***(positive)	**(positive)	***(positive)	***(positive)	***(negative)	***(positive)
No. of years since dementia diagnosis	NS	NS	NS	NS	NS	NS

† Primary independent variable
Abbreviations: NS, not significant; CHD, coronary heart disease.
P values: *p≤0.05;**p≤ 0.01;*** p≤ 0.001

APPENDIX D.3: Results of non-weighted bivariate analyses for all possible specifications of dementia status for study aim 3

Dementia Measure	ACE Inhibitors	Beta-blockers	Lipid -lowering Medications	Antiplatelet Medications
No. of years since dementia diagnosis †	NS	***(negative)	NS	**(negative)
3MSE Score Less than 80	NS	NS	NS	**(negative)
DSST Score Less than 30	NS	NS	NS	**(negative)

† Primary independent variable
Abbreviations: NS, not significant; 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test.
P values: P values: *p≤0.05;**p≤ 0.01;*** p≤ 0.001.

APPENDIX E

RESULTS OF NON-WEIGHTED BIVARIATE ANALYSES

E.1: Results of Non-Weighted Bivariate Analysis of Chemoprophylaxis for CHD in Participants with Dementia and CHD (AIM 1)

Variable	ACE Inhibitors		Beta-blockers		Lipid-lowering Medications		Antiplatelet Medications	
Predisposing variables	**β coefficient**	**OR**	**β coefficient**	**OR**	**β coefficient**	**OR**	**β coefficient**	**OR**
Dementia (in that year)	0.227**	1.26	-0.128	0.88	-0.080	0.92	-0.087	0.92
Dementia at baseline	-0.461	0.63	-1.125**	0.33	-1.000*	0.37	-0.600**	0.55
Prevalent dementia	0.206	1.23	-0.841***	0.43	-1.450***	0.23	-0.389*	0.68
3MSE Score <=80	-0.031	0.97	-0.030	0.97	-0.220*	0.80	-0.184*	0.83
DSST Score <=30	0.215**	1.24	-0.083	0.92	-0.102	0.90	-0.232***	0.79
Age centered on the mean	0.430***	1.04	-0.025**	0.98	0.008	1.01	-0.163*	0.98
Age categories (≤75)	0.166**	1.18	-0.074**	0.93	-0.220*	0.80	-0.671	0.94
76-85								
86-102	0.343	1.41	-0.213	0.81	-0.102	0.90	-0.390**	0.68
Age and dementia interaction	0.013	1.01	0.041	1.00	-0.026	0.97	-0.004	1.00
Study site (North Carolina)								
California	-0.019	0.98	-0.293	0.74	-0.046	0.95	-0.133*	0.73
Maryland	0.077	1.08	-0.227	0.79	-0.266	0.76	-0.375*	0.68
Pennsylvania	0.305	0.73	-0.121	0.88	-0.270	0.76	-0.177	0.83
Race (white)	-0.010	0.99	0.001	1.00	0.278	1.32	0.342**	1.41
Gender (male)	0.381**	1.46	-0.188**	0.83	-0.142	0.87	0.433***	1.54
Education (HS or less)	0.081	1.08	-0.029	0.97	0.050	1.05	-0.068	0.93
Enabling Variables								
Income (<$24,999/year)	-0.463	0.76	-0.226	0.80	-0.422**	0.66	-0.453***	0.636
Insurance status (none)								
Private	-0.010	0.98	0.143	1.15	-0.038	0.96	0.206	1.22
Medicaid	-0.067	0.93	-0.105	0.90	-0.331	0.71	0.257	1.29
Other	0.064	1.06	0.186	1.20	0.057	1.05	0.199	1.22
Ever had private insurance	-0.163	0.84	0.284	1.32	0.379	1.46	0.428	1.53
Ever had Medicaid	-0.125	0.88	-0.177	0.83	-0.094	0.91	-0.356**	0.70
Ever had other insurance	0.049	1.05	0.057	1.05	0.251	1.28	-0.005	0.99
Ever without insurance	0.144	1.15	-0.138	0.87	-0.234	.079	-0.361**	0.69
Residing in Nursing Home	0.660**	1.93	-0.153	0.86	-0.215	0.81	-0.500	0.61
Care Need Variables								
Activities of daily living	0.080**	1.082	0.005	1.01	-0.050	0.95	-0.137***	0.87
Hypertension	0.222***	1.25	0.116***	1.12	0.105***	1.11	0.005	1.00
Diabetes	0.156***	1.17	-0.076	0.93	0.010	1.01	-0.137	0.87
Renal Insufficiency	0.371*	1.45	0.104	1.11	0.007	1.01	0.037	1.04
Ever treated for Cancer	0.027	1.03	0.247	1.28	-0.135	0.87	-0.066	0.94

Abbreviations: 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test; CHD, Coronary Heart Disease.
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

E.2: Results of Non-Weighted Bivariate Analysis of Chemoprophylaxis for CHD in Participants with Dementia before CHD (AIM 2)

Variable	ACE Inhibitors		Beta-blockers		Lipid lowering Medications		Antiplatelet Medications	
Predisposing variables	β coefficient	OR	β coefficient	OR	β coefficient	OR	β coefficient	OR
Dementia before CHD	-0.346	0.71	-0.663*	0.52	-1.369**	0.25	-0.747***	0.47
Disease status each year (none)								
CHD only	0.875**	2.40	1.134***	3.11	1.500**	4.48	1.010***	3.00
Dementia only	0.236	1.27	-0.396	0.96	0.384	1.47	0.409	1.50
Both diseases	1.111***	3.04	1.073**	2.93	1.710***	5.53	1.172***	3.23
No. of years since dementia diagnosis	0.102**	1.11	-0.022	0.98	0.487	1.05	0.014	1.01
Age centered on the mean	0.292	1.03	-0.005	0.99	0.128	1.01	0.020	1.02
Age categories (≤75)	0.142	1.15	-0.347	0.97	0.322	1.38	0.139	1.15
76-85								
86-102	0.087	1.10	-0.074	0.93	0.847	1.09	0.239	1.27
Age and dementia interaction	-0.008	0.99	0.215	1.02	-0.158	0.98	0.020	1.02
Study site (North Carolina)								
California	-0.212	0.81	-0.103	0.90	-0.457	0.63	-0.270	0.76
Maryland	-0.077	0.93	-0.121	0.89	-0.339	0.71	-0.400	0.67
Pennsylvania	-0.539	0.58	0.024	1.02	-0.520	0.59	-0.336	0.71
Race (white)	-0.164	0.85	0.470	1.60	-0.317	0.73	0.571**	1.77
Gender (male)	0.543*	1.72	-0.061	0.94	-0.235	0.79	0.646***	1.91
Education (HS or less)	0.014	1.01	-0.052	0.95	-0.123	0.88	-0.162*	0.85
Enabling Variables								
Income (<$24,999/year)	0.003	1.00	-0.293	0.75	-0.153	0.86	-0.657***	0.52
Insurance status (none)								
Private	0.065	1.07	0.310	1.36	-0.120	0.89	0.179	1.20
Medicaid	0.117	1.12	0.132	1.14	-0.028	0.97	-0.028	0.97
Other	0.312	1.37	0.387*	1.47	-0.043	0.96	0.154	1.17
Ever had private insurance	-0.404	0.67	0.739*	2.09	0.925	2.52	0.468*	1.60
Ever had Medicaid	-0.221	0.98	-0.151	0.86	0.350	1.42	-0.384	0.68
Ever had other insurance	0.204	1.23	0.290	1.34	-0.193	0.82	0.163	1.18
Ever without insurance	0.139	1.15	-0.441	0.64	0.074	1.08	-0.467**	0.63
Residing in Nursing Home	-0.403	1.50	-0.041	0.96	-0.357	0.70	-0.268	0.76
Care Need Variables								
Activities of Daily Living	0.070*	1.07	-0.003	1.00	-0.070	0.93	-0.028	0.97
Hypertension	0.118*	1.13	0.151	1.16	0.030	1.03	-0.026	0.97
Diabetes	0.206**	1.23	0.002	1.00	0.040	1.04	0.052	1.05
Renal Insufficiency	0.452	1.57	-0.256	0.77	-0.320	0.73	0.250	1.28
Any arthritis	-0.192**	0.83	-0.904	0.91	-0.019	0.98	-0.177	0.84
Ever treated for Cancer	0.218	1.24	-0.193	0.82	-0.147	0.87	-0.039	0.96

Abbreviations: CHD, Coronary Heart Disease; No., number; HS, high school. P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

E.3:**Results of Non-Weighted Bivariate Analysis of Chemoprophylaxis Discontinuation for CHD in Participants with Dementia after CHD (AIM 3)**

Variable	ACE Inhibitors		Beta-blockers		Lipid lowering Medications		Antiplatelet Medications	
Predisposing variables	β coefficient	OR	β coefficient	OR	β coefficient	OR	β coefficient	OR
No. years since dementia diagnosis	–0.145	0.86	–0.261***	0.77	–0.217	0.81	–0.145**	0.87
3MSE Score <=80	–0.479	0.62	0.043	1.04	–0.430	0.65	–0.435**	0.65
DSST Score <=30	–0.833	0.43	–0.272	0.76	0.213	1.24	–0.562**	0.57
Age centered on the mean	–0.146**	0.86	–0.134***	0.87	–0.089	0.92	–0.067***	0.93
Age categories 76-85	0.002	1.00	–0.418	0.66	–0.528	0.59	–0.509*	0.60
86-102	–1.782**	0.17	–1.162*	0.31	–1.254*	0.29	–0.954**	0.39
Age and yrs since dementia interaction	–0.071*	0.93	–0.060**	0.94	–0.122	0.99	–0.043	0.96
Study Site								
Davis	–0.538	0.58	–0.461	0.63	–0.998	0.37	–0.597	0.55
Hopkins	–0.263	0.77	–0.591	0.55	–0.441	0.64	–0.456	0.63
Pittsburgh	–0.700	0.50	–0.090	0.91	–0.419	0.66	–0.282	0.75
Race	–0.064	0.94	–0.216	0.81	–0.218	0.80	0.242	1.28
Gender	0.859	2.36	–0.035	0.97	1.168*	3.21	0.684***	1.98
Education (HS or less)	–0.316	0.73	–0.075	0/93	0.302	1.35	–0.163	0.85
Enabling Variables								
Income (<$24,999/year)	0.107	1.11	0.300	1.34	–0.484	0.62	–0.505*	0.60
Insurance status								
Private	0.669	1.95	0.449	1.57	0.190	1.21	–0.072	0.93
Medicaid	0.586	1.06	0.043	1.04	0.916***	2.50	–0.191	0.83
Other	1.192	3.29	0.441	1.55	0.279	1.32	–0.091	0.91
Ever had private insurance	0.298	1.35	0.409	1.51	1.079***	2.94	0.488*	1.63
Ever had Medicaid	–0.185	0.83	0.191	1.21	1.512	4.54	–0.630	0.53
Ever had other insurance	0.029	1.03	0.146	1.16	0.074	1.08	0.127	1.14
Ever had no secondary ins	0.113	1.12	–0.219	0.80	–0.217	0.80	–0.246	0.78
Residing in Nursing Home	–0.286	0.75	–0.465	0.96	–0.020	0.97	–1.228**	.029
Care Need Variables								
Activities of Daily Living	–.0479	0.95	–0.128**	0.88	–0.204*	0.82	–0.216	0.81
No of yrs since CHD	–0.193**	0.82	–0.255***	0.77	–0.156	0.86	–0.203	0.82
CHD at baseline	0.433	1.54	0.240	1.27	0.600	1.82	0.186	1.02
Hypertension	–0.148	0.86	0.049	1.05	–0.216	0.81	–0.374	0.69
Diabetes	–0.038	0.96	–0.134	0.87	0.447*	1.56	–0.236	0.79
Renal Insufficiency	–0.091	0.91	–0.500	0.61	–0.344	0.71	–0.843	0.92
Ever treated for Cancer	0.010	1.01	0.055	1.06	0.858	2.36	0.280	1.32
Any arthritis	–0.156	0.86	–0.064	0.94	–0.048	0.95	–0.087	0.92

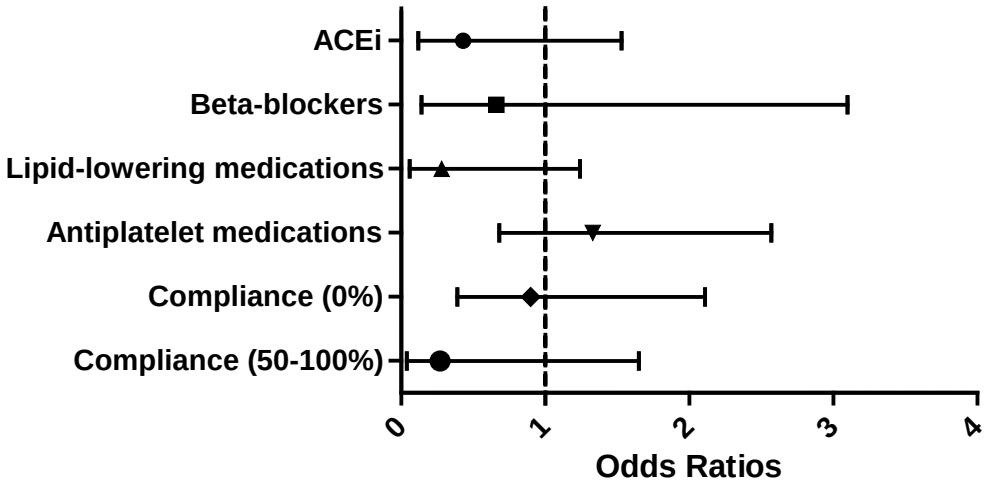
Abbreviations: 3MSE, Modified Mini-Mental State Examination; DSST, Digit Symbol Substitution Test; CHD, Coronary Heart Disease.
P values: *p≤ 0.05; **p≤0 .01;*** p≤0.001.

APPENDIX F

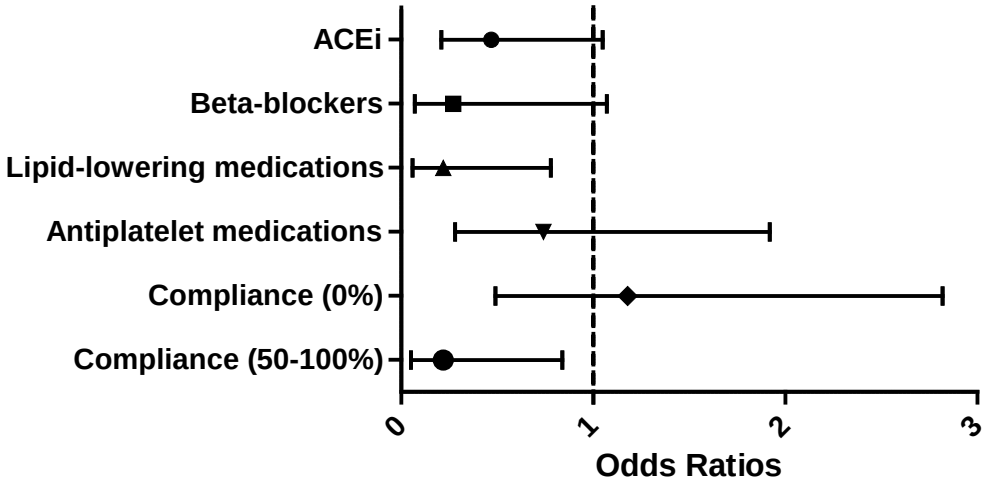
ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR USE OF CHEMOPROPHYLAXIS FOR PARTICIPANTS WITH CHD AND DEMENTIA USING ALTERNATIVE SPECIFICATIONS OF INDEPENDENT VARIABLE

F.1: Dementia at Baseline

FULL MODEL

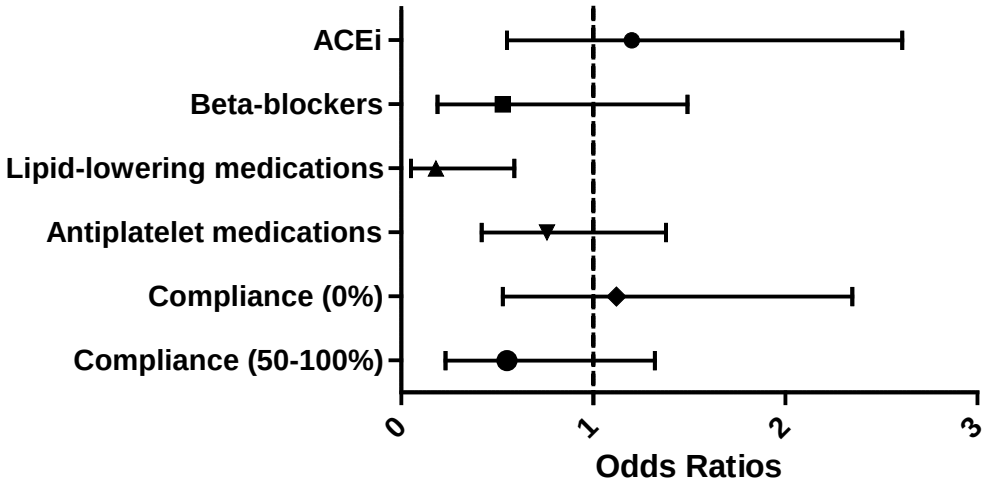


FINAL MODEL

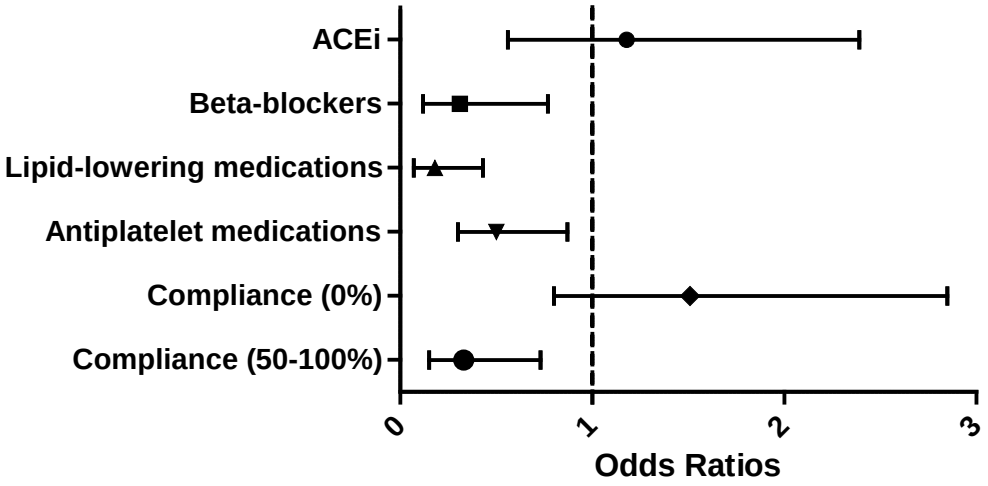


F.2 : Prevalent Dementia

FULL MODEL

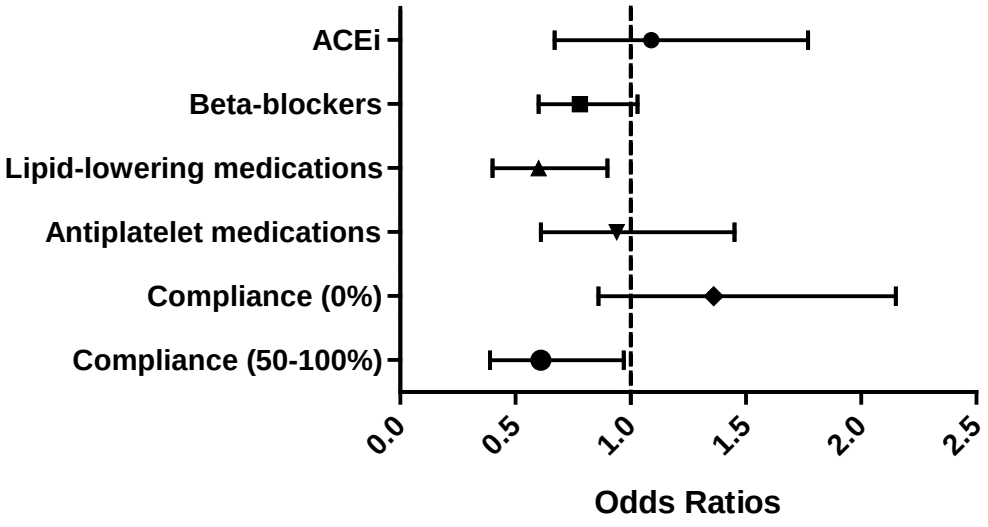


FINAL MODEL

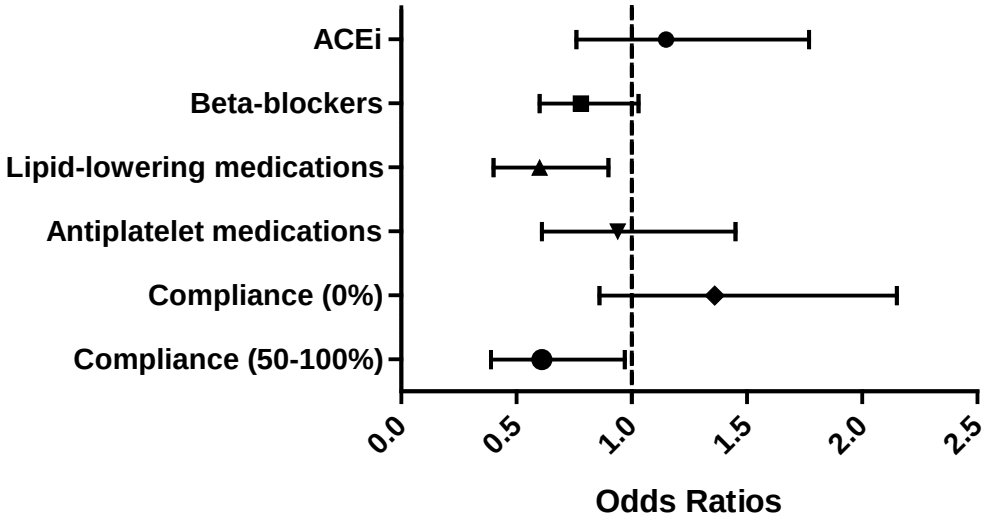


F.3: 3MSE SCORE <80

FULL MODEL

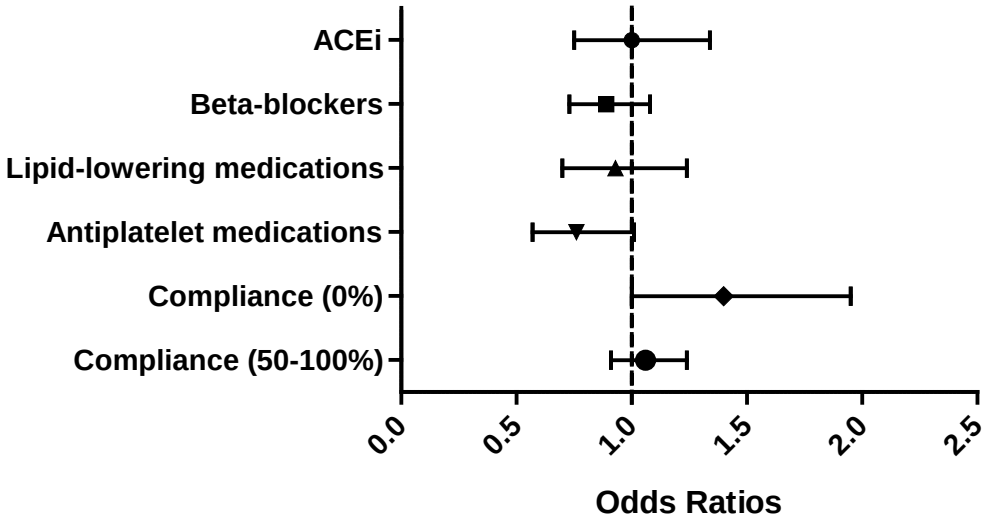


FINAL MODEL

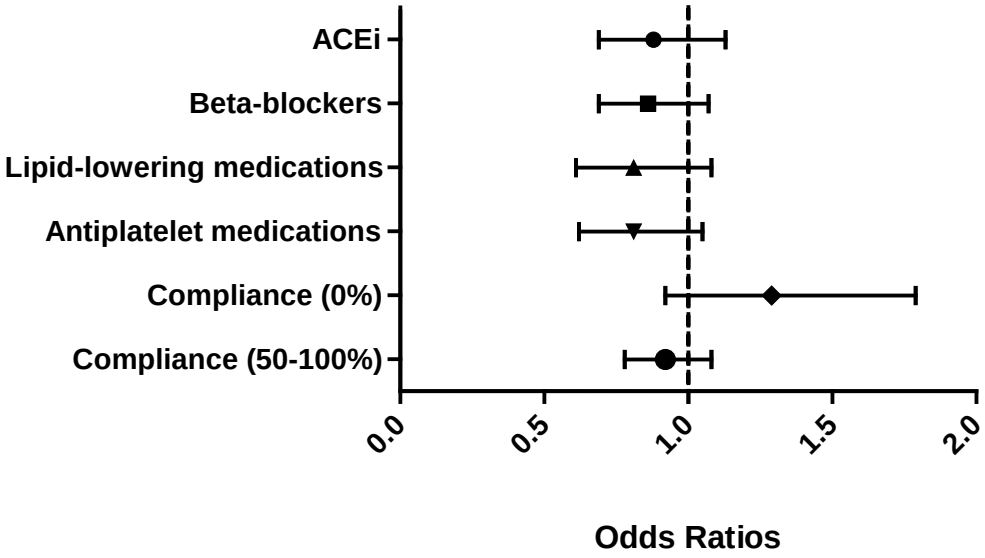


F.4: DSST Score <30

FULL MODEL



FINAL MODEL

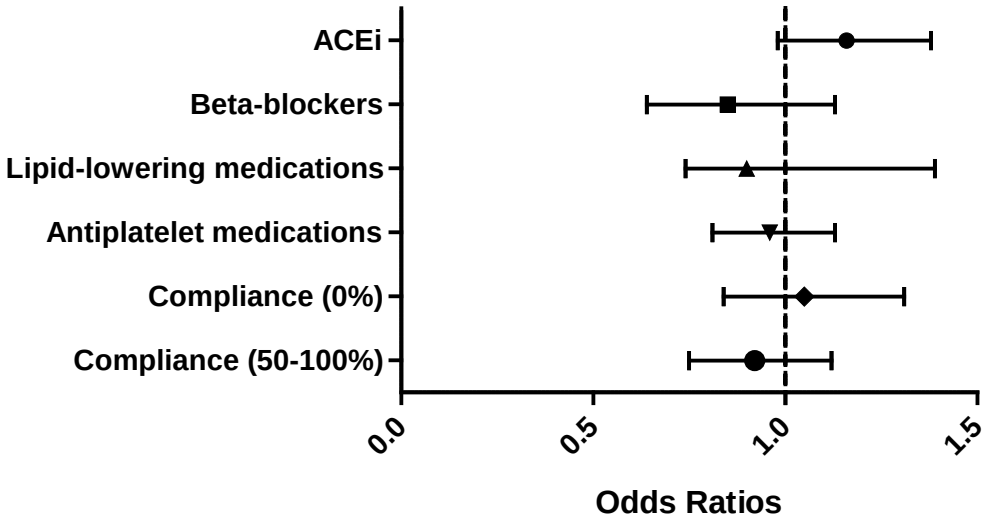

ACEi
Beta-blockers
Lipid-lowering medications
Antiplatelet medications
Compliance (0%)
Compliance (50-100%)
0.0
0.5
1.0
1.5
2.0
Odds Ratios

APPENDIX G

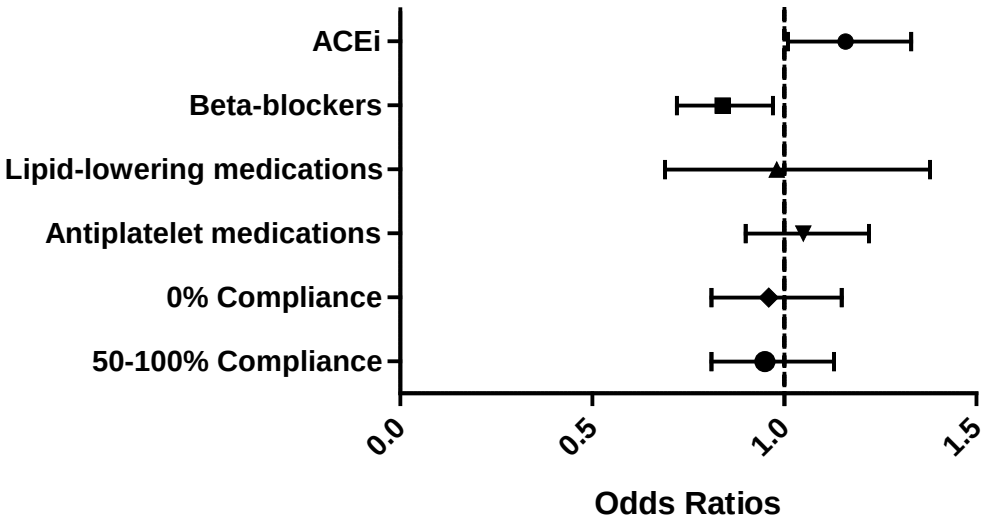
ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR USE OF CHEMOPROPHYLAXIS FOR PARTICIPANTS WITH DEMENTIA BEFORE CHD USING ALTERNATIVE SPECIFICATIONS OF INDEPENDENT VARIABLE

G.1: Number of years with Dementia

FULL MODEL



FINAL MODEL

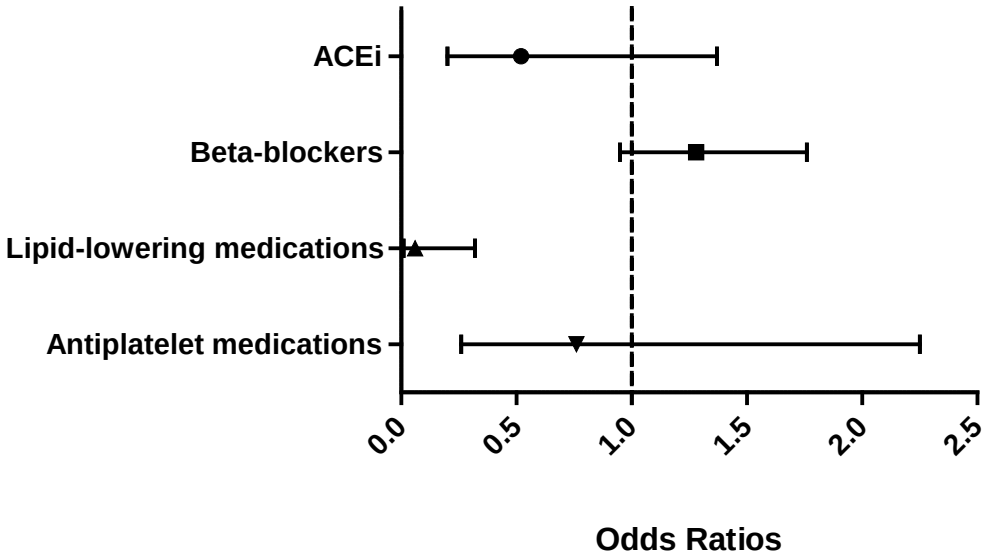

ACEi
Beta-blockers
Lipid-lowering medications
Antiplatelet medications
0% Compliance
50-100% Compliance
0.0
0.5
1.0
1.5
Odds Ratios

APPENDIX H

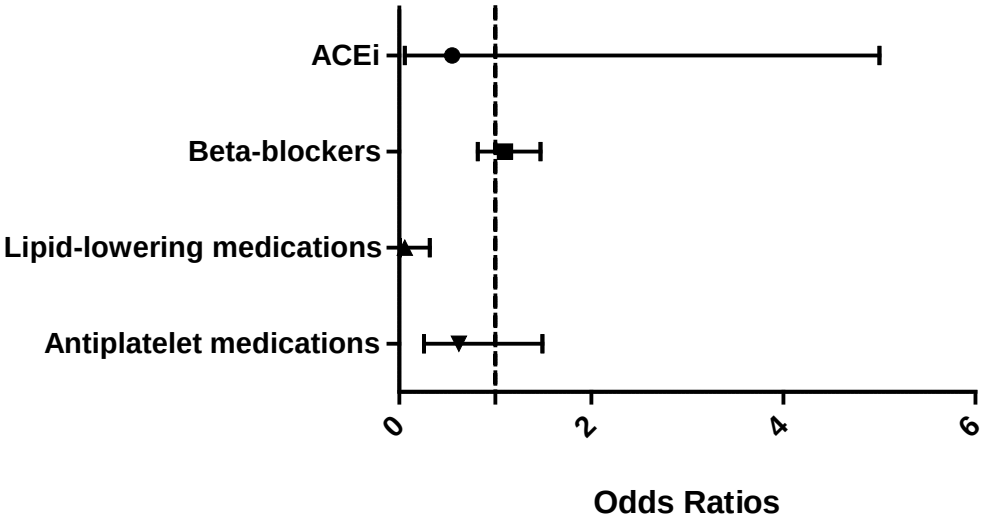
ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR DISCONTINUATION OF CHEMOPROPHYLAXIS FOR PARTICIPANTS WITH DEMENTIA AFTER CHD USING ALTERNATIVE SPECIFICATIONS OF INDEPENDENT VARIABLE

H.1 3MSE SCORE <80

FULL MODEL



FINAL MODEL


ACEi
Beta-blockers
Lipid-lowering medications
Antiplatelet medications
0
2
4
6
Odds Ratios

BIBLIOGRAPHY

Adams WL, McIlvain HE, Geske JA, Porter JL. Physicians' Perspectives on Caring for Cognitively Impaired Elders *The Gerontologist* 2005;45:231-239.

Albert SM, Del Castillo-Castaneda C, Sano M, et al. Quality of life in patients with Alzheimer's disease as reported by patient proxies. *J Am Geriatr Soc* 1996;44:1342–1347.

Alzheimer's Association. Alzheimer's disease facts and figures 2007. http://www.alz.org/national/documents/report_alzfactsfigures2007. pdf. Accessed October 19, 2009.

American Heart Association. *Heart Disease and Stroke Statistics — 2004 Update*. Dallas, Tex.: American Heart Association; 2003. http://www.americanheart.org/downloadable/heart/1079736729696HDSStats2004Update REV3-19-04.pdf Accessed on November 3, 2009.

Andersen RM, Newman JF. Societal and individual determinants of medical care utilization in the United Status. *Milbank Q* 1973;51(1):203–209.

Andersen RM. Revisiting the behavioral mode and access to medical care. Does it matter? *J Health Soc Behav* 1995;36(1):1–10.

Anderson KL, Burckhardy CS. Conceptualization and measurement of quality of life as an outcome variable for health care intervention and research. *J Adv Nurs* 1999;29(2):298–306.

Antiplatelet Trialists' Collaboration. Secondary prevention of vascular events by prolonged antiplatelet therapy. *Br Med J* 1988;296:320–331.

Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *Br Med J* 2002;324;71–86.

Baiker K, Chandra A, Skinner JS. Geographic variation in health care and the problem of measuring racial disparities. *Perspect Biol Med* 2005;48(1):S42–S53.

Balkrishnan R. Predictors of medication adherence in the elderly *Clinical Therapeutics* 1998:(20)4; 764-771.

Beauchamp T., Childress J. *Principles of Biomedical Ethics.* 2008 Oxford University of Press.

Beers MH, Ouslander JG, Fingold SF, et al. Inappropriate medication prescribing in nursing facilties. *Ann Intern Med* 1992;1117:684–689.

Beers MH, Ouslander JG, Fingold SF, et al. Psychoactive medication use in intermediate care facility residents. *JAMA* 1988;260:3016–3020.

Benner JS, Glynn RG, Mogun H, et al. Long-term persistence in use of statin therapy in elderly patients *JAMA* 2002;288:455–461.

Berlowitz DR, Du W, Kazis L, Lewis S. Health-related quality of life of nursing home residents: Differences in patient and provider perceptions. *J Am Geriatr Soc* 1995 Jul;43(7):799-802.

Blass DM, Black BS, Phillips H, et al. Medication use in nursing home residents with advanced dementia. *Int J Geriatr Psychiatry* 2008; 23:490–496.

Boustani M, Peterson B, Hanson L, et al. Screening for dementia in primary care: a summary of the evidence for the U.S. Preventative Services Task Force. *An of Int Med.* 2003b;138:927–37.

Boyd CM, Darer J, Coult D, Fried LP, Boult L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases. *JAMA* 2005;294:716-724.

Bradley EH, McGraw SA, Curry L, Buckser A, King KL, Kasl SV, Ansersen R. Expanding the Andersen Model: the role of psychosocial factors in long-term care use. HSR. 2002:37(5) 1221-1242.

Braithwaite RS, Concato J, Chang CC, Roberts MS, Justice AC. A framework for tailoring clinical guidelines to comordbity at the point of care. *Arch Int Med* 2002;167(21):2361-2365.

Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. *Neuropsy Be*. 1988;1:111-117.

Brauner DJ, Muir JC, Sachs GA. Treating nondementia illnesses in patients with dementia. *JAMA* 2000;283(24):3230–3235.

Briesacher B, Limcangco R, Gaskin D. Racial and ethnic disparities in prescription coverage and medication use. *Health Care Financ Rev* 2003 Winter;25(2):63–76.

Brock DW. Life and death: Philosophical essays in biomedical ethics 1994. Cambridge University Press.

Brock, DW. Quality of life measures in health care and medical ethics. In: A. Sen and M.C. Nussbaum, Editors, *The Quality of Llife*, Oxford University Press, New York (1993), pp. 133–165.

Byrne M, Walsh J, Murphy AW. Secondary prevention of coronary heart disease: Patient beliefs and health-related behaviour. *J Psychosom Res* 2005;58:403–415.

Callahan D. When Self-Determination Runs Amok *The Hastings Center Report* 1992;22(2):52-55.

CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996;348(9038):1329–1339.

Carmines EG, Zeller RA. *Reliability and Validity Assessment* Beverly Hills, CA: Sage, 1979.

Carter BL, Malone DC, Ellis SL, Dombrowski RC. Antihypertensive drug utilization in hypertensive veterans with complex medication profiles. *J Clin Hypertens* 2000;2:172–180.

Chadda K, Goldstein S, Byington R, Curb JD. Effect of propranolol after acute myocardial infarction in patients with congestive heart failure. *Circulation* 1986;73;503–510.

Charles C, Gafni A, Whelan T. Shared decision-making in the medical encounter: What does it mean? *Soc Sci Med* 1997;44:681–692.

Chassin MR, Kosecoff, J, Park RE, Winslow CM. Does inappropriate use explain geographic variations in the use of health services. *JAMA* 1987;258(18):2533-2537.

Chodosh J, Petitti DB, Elliott M. et al. Physician recognition of cognitive impairment: Evaluation the need for improvement. *JAGS* 2004;52:1051-1059.

Chrischilles EA, Foley DJ, Wallace RB, et al. Use of medications by persons 65 and over: Data from the Established Populations of Epidemiologic Studies of the Elderly. *J Gerontol* 1992;47:M137–144.

Claesson S, Morrison A, Wertheimer AI, Berger ML. Compliance with prescribed drugs: challenges for the elderly population. *Pharm World Sci* 1999;21(6): 256-259.

Cline CM, Björck-Linné BA, Willenheimer RB, Erhardt LR. Non-compliance and knowledge of prescribed medication in elderly patients with heart failure. *European Journal of Heart Failure* 1999;1(2): 145-149.

Col N, Fanale JE, Kornhom P. The role of medication noncompliance and adverse drug reactions in the elderly. *Arch Int Med*. 1990;150:841-845.

Coleman EA, Feuer EF, and the NCI Breast Cancer Screening Consortium. Breast cancer screening among women age 65 to 74 years of age in 1987–88 and 1991. *Ann Intern Med* 1992;117:961–966.

Collins R, Armitage J, Parish S, et al; Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: A randomised placebo-controlled trial. *Lancet* 2003;361(9374):2005–2016.

Coons SJ, Shehan SL, Martin SS. Predictors of medication noncompliance in a sample of older adults. *Clin Ther* 1994;16:110–117.

Cooper A, Lloyd G, Weinman J. Why patients do not attend cardiac rehabilitation: Role of intentions and illness beliefs. *Heart* 1999;82:234–236.

Cooper JK, Love DW, Raffoul PR. Intentional prescription nonadherence (non-compliance) in the elderly. *JAGS* 1982;30:329-333.

Cooper LA, Hill MN, Powe NR. Designing and evaluating interventions to eliminate racial and ethnic disparities in health care. *J Gen Intern Med* 2002;17:477–486.

Corrada M, Brookmeyer R, Kawas C. Sources of variability in prevalence rates of Alzheimer's disease. *Int J Epidemiol* 1995;24:1000-5.

Crane D. Sanctity of Social Life: Physicians' Treatment of Critically Ill Patients. New York, Russell Sage Foundation, 1975.

Ditto PH, Danks JH, Smucker WD, Bookwala J, Coppola KM, Dresser R, Fagerlin A, Gready M, Houts RN, Lockhart LK, Zyzanski S. Advance Directives as Acts of Communication. *Arch Intern Med.* 2001;161:421-430.

Dooley N, Hinojosa J. Improving quality of life for persons with Alzheimer's disease and their family caregivers: Brief occupational therapy intervention. *Am J Occup Ther* 2004;58:561–569.

Dunkin JJ, Anderson-Hanley C. Dementia caregiver burden: A review of the literature and guidelines for assessment and intervention. *Neurology* 1998;51(1 Suppl 1):S53–60.

Eaker E, Mickel SF, Chyou P. Alzheimer's disease or other dementia and medical care utilization. *Ann Epidemiol* 2002;12(1):39–45.

Eddy DM. Clinical decision making: From theory to practice—anatomy of a decision *JAMA* 1990;263(3):441–443.

Eddy, DM. Variations in physician practice: the role of uncertainty. *Health affairs* 1984;3(2):74.

Eisenberg J. Sociologic influences on decision-making by clinicians. *Ann Intern Med* 1979;90:957–964.

Engelhardt HT. The Foundations of Bioethics, 2nd edition. Oxford and New York: Oxford University Press, 1996.

Federman AD, Adams AS, Ross-Degnan D, et al. Supplemental insurance and use of effective cardiovascular drugs among elderly Medicare beneficiaries with coronary heart disease. *JAMA* 2001;286(14):1732–1739.

Field TS. Gurwitz JH, Harrold LR, Rothschild J, DeBellis KR, Seger AC, Auger JC, Garber LA, Cadoret C, Fish LS, Garber LD, Kelleher M, Bates DW. *JAGS* 2004(52);8:1349-1354.

Fillenbaum GC, Hanlon JT, Corder EH, Ziqubu-Page T. Prescription and nonprescription drug use among black and white community residing elders. *Am J Public Health* 1993;83:1577–1582.

Fischer, E., Wennberg D, Stukel TA, Gottlieb DJ, Luca FL, Pinder E. The Implications of regional variations in Medicare spending. Part 2: Health outcomes and satisfaction with care *Ann Intern Med* 2003;138 (4) 288-298

Fitzmaurice GM. A caveat concerning independence estimating equations with multivariate binary data. *Biometrics* 1995; 51:309-317.

Flather MD, Lonn EM, Yusuf S. Effects of ACE inhibitors on mortality when started in the early phase of myocardial infarction: Evidence from the larger randomized controlled trials. *J Cardiovasc Risk* 1995;2:423–428.

Flood, AB, Wennberg J, Nease R, Fowler F. The importance of patient preference in the decision to screen for prostate cancer *JGIM* 1995;11(6); 342-349.

Folstein MF, Folstein SE, McHugh PR. Mini-mental state: A practical method for grading the cognitive state of patients for the clinician". *J of Psych Res* 1975;3:189–98.

Fox E. Predominance of the curative model of medical care: A residual problem. *JAMA* 1997;278:761-764.

Frampton M. Experience assessment and management of pain in people with dementia. *Age and Ageing* 2003; 32: 248–251

Fried TL, Bradlety EH, Towle VT, Allore H. Understanding the treatment preferences of seriously ill patients *N Engl J Med* 2002;346(14):1061–1066.

Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;274(6):462.

Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA. Causes and consequences of comorbidity: a review. *J Clin Epidemiol.* 2001 Jul;54(7):661-74.

Giugliano RP, Braunwald E. 2004 ACC/AHA guideline for the management of patients with STEMI: The implications for clinicians. *Nat Clin Pract Cardiovasc Med* 2005 Mar;2(3):114–115.

Gorin S, Heck J, Albert S, Hershman D. Treatment for Breast Cancer in Patients with Alzheimer's Disease *JAGS* 2005;53(11):1897-1904.

Gornick ME, Eggers PW, Reilly TW, et al. Effects of race and income on mortality and use of services among Medicare beneficiaries. *N Engl J Med* 1996;335:791–799.

Gupta SK, Lamont EB. Patterns of presentation, diagnosis, and treatment in older patients with colon cancer and comorbid dementia. *JAGS* 2004(52);10:1681-1687.

Hanlon JT, Fillenbaum GG, Burchett B, Wall WE, Service C, Blazer DG, George LK. Drug-use patterns among black and nonblack community-dwelling elderly. *The Annals of Pharmacotherapy* 1992;(26)5:679-685.

Hanlon JT, Landerman LR, Wall WE, Horner RD, Fillenbaum GG, Dawson DV, Schmader KE, Cohen HJ, Blazer DJ. Is Medication Use by Community-dwelling Elderly People Influenced by Cognitive Function? *Age and Ageing* 1996;25(3): 190-196.

Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *Am J of Geriatric Pharmacotherapy* 207;5:345-351.

Hawkins NA, Ditto PH, Danks JH, Smucker WD. Micromanaging death: Process preferences, values, and goals in end-of-life medical decision making. *Gerontologist* 2005;45(1):107–117.

Heflin M, Oddone EZ, Pieper CE, et al. The effect of comorbid illness on receipt of cancer screening by older people. *J Am Geriatr Soc* 2002;50:1651–1658.

Hoffman C, Rice D, Sung HY. Persons with chronic conditions: Their prevalence and costs. *JAMA* 1996;276(18):1473–1479.

Holmes HM, Haley, DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. *Arch Int Med* 2006;166:605-608.

Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA guidelines for the diagnosis and management of chronic heart failure in the adult: A report of the American College of Cardiology/ American Hearth Association Task Force on Practice Guidelines (Committee on the evaluation and management of heart failure). *J Am Coll Cardiol* 2005;46:1116–1143.

Ives DG**,** Lave JR, Traven ND, Schulz R, Kuller LH. Mammography and Pap smear use by rural older women. *Public Health Reports* 1996;III:244-250.

Jha AK, Varosy PD, Kanaya AK, et al. Differences in medical care and disease outcomes among black and white women with heart disease. *Circulation* 2003;108:1089–1094.

Johnson H, Bouman WP, Pinner G. On telling the truth in Alzheimer's disease: A pilot study of current practice and attitudes. *Int Psychogeriatr* 2000;12:221–229.

Jorm AF, Jacomb PA. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): Socio-demographic correlates, reliability, validity and some norms. *Psych Med* 1989;19:1015-1022.

Kaplan GA. Socioeconomic factors and cardiovascular disease: A review of the literature. *Circulation* 1993;88:1973–1998.

Karlawish JH, Casarett DJ, James BD. Alzheimer's disease patients' and caregivers' capacity, competency, and reasons to enroll in an early-phase Alzheimer's disease clinical trial. *J Am Geriatr Soc* 2002;50:2019–2024.

Kaiser Permanente Care Management Institute. Adult diabetes clinical practice guidelines. Oakland (CA): Kaiser Permanente Care Management Institute; 2005 Dec. 206 p.

Karnath B. Subdural hematoma: Presentation and management in older adults. Geriatrics

2004; 58(July):18-23.

Kayser-Jones J, Weiner CL, Barbaccia JC. Factors contributing to the hospitalization of nursing home residents. *Gerontologist* 1989;29:502–510.

Kiefe C, Funkhouser E, Fouad M, May D. Chronic disease as a barrier to breast and cervical cancer screening. *J Gen Intern Med* 1998;13(6):357–365.

Kistler, CE, Lewis CL, Amick HR, Bynum DL, Walter LC, Warsom LC. Older adults' beliefs about physician-estimated life expectancy: a cross sectional survey. *BMC Fam Practice* 2006:7:1-6.

Kravitz RL, Epstein RM, Feldman MD. Influence of patients' requests for direct-to-consumer advertised antidepressants: a randomized controlled trial. *JAMA* 2005;293:1995-202.

Krumholz HM, Radford MJ, Wang Y, et al. National use and effectiveness of β-blockers for the treatment of elderly patients after acute myocardial infarction: National Cooperative Cardiovascular Project. *JAMA* 1998;280:623–629.

Kuller LH, Shemanski L, Manolio T, Haan M, Fried L, Bryan N, Burke,GL, Tracy R, Bhadelia R. Relationship Between ApoE, MRI Findings, and Cognitive Function in the Cardiovascular Health Study *Stroke.* 1998;29:388-398.

Landi F, Gambassi G, Lapane KL, Sgadari A, Gifford D, Mor V, Bernabei R. Comorbidity and Drug Use in Cognitively Impaired Elderly Living in Long-Term Care. *Dement Geriatr Cogn Disord* 1998;9:347-356

Larson EB, Shadlen MF, Wang L. Survival after initial diagnosis of Alzheimer's disease. *Ann Intern Med* 2004; 140:501-509.

Lawton, MP. A multidimensional view of quality of life in frail elders. In: Birren JE et al. (Eds). *The Concept and Measurement of Quality of Life in the Frail Elderly*. San Diego: Academic Press, 1991, pp 3–27.

Lawton MP. Assessing quality of life in Alzheimer disease research. *Alzheimer Dis Assoc Disord* 1997;11(Suppl 6):91–99.

Leventhal H, Meyer D, Nerenz D. The common sense representation of illness danger. In: Rachman S (Ed). *Medical Psychology*. Vol 2. New York: Pergamon, 1980, pp 7–30.

Lewis SJ, Moye LA, Sacks, FM. Effect of pravastatin on cardiovascular events on older persons with myocardial infarction and cholesterol levels in average ranges. *Ann Intern Med* 1998;129:681–689.

Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73: 13–22.

Lin OS, et al. Screening colonoscopy in very elderly patients: prevalence of neoplasia and estimated impact on life expectancy. *JAMA* 2006;295:2357–65.

Lipton HL, Lee PR (Eds). Drugs and the Elderly: Clinical, Social, and Policy Perspectives. Stanford University Press, 1988.

Logsdon RG, Gibbons LE, McCurry SM, Fried L. Assessing Quality of Life in Older Adults With Cognitive Impairment *Psychosomatic Medicine* 2002;64:510-519.

Lopez, O. Personal communication. 2008

Lopez OL, Kuller LH, Fitzpatrick A, Ives D, Becker JT, Beauchamp N. Evaluation of Dementia in the Cardiovascular Health Cognition Study. *Neuroepidemiology* 2003;22:1-12.

Lopez OL, Jagust WJ, Dulberg C, et al. Risk factors for mild cognitive impairment in the Cardiovascular Health Study Cognition Study: part 2. *Arch Neurol.* 2003;60:1394-1399

Lopez OL, Becker JT, Klunk W, et al. Research evaluation and diagnosis of probable Alzheimer's disease over the last two decades: I. Neurology 2000;55:1854–1862.

Lubeck DP, Hubert HB. Self-report as a viable method for obtaining health care utilization data in community-dwelling seniors *J of Clini Epid* 2005;58: 286-290

Lynn J, Degrazia D. An outcomes model of medical decision making. *Theoretical Medicine and Bioethics* 12 (4).

Magaziner J, German P, Zimmerman S, et al. The prevalence of dementia in a statewide sample of new nursing home admissions aged 65 and older: Diagnosis by expert panel. *Gerontologist* 2000;40:663–672.

Marwill SL, Freund KM, Barry PP. Patient factors associated with breast cancer screening among older women. *J Am Geriatr Soc* 1996;*44*: 1210–4.

Maslow K. Use of Medicare services and Medicare costs for people with Alzheimer's disease and other dementias. 1999 Alzheimer's Association White paper.

Mast KR, Salama MB, Silverman GK, Arnold RM. End-of-Life Content in Treatment Guidelines for Life-Limiting Diseases *J of Pall Med.* 2004, 7(6): 754-773

McCormick WC, Hardy J, Kukull WA, Bowen JD, Teri L, Zitzer S, Larson EB. Healthcare utilization and costs in managed care patient with Alzheimer's disease during the last few years of life. *JAGS* 2001;49:1156-1160.

McCrary SV, Swanson JW, Younger SJ, et al. Physicians quantitative assessment of medical futility. *J Clin Ethics* 1994;5:100–105.

McCulloch CE, Searle SR. Generalized, Linear, and Mixed Models, John Wiley Sons Inc, New York, New York (2001).

McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDSADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34:939-44.

McLaughlin TJ, Soumerai SB, Willison DJ, Gurwitz JH, Borhas C., Guadagnoli E., McLaughlin B., Morris N., Cheng SC, Hauptman PJ, Antman E., Casey L., Asinger R., Gobel F., Adherence to national guidelines for drug treatment of suspected acute myocardial

infarction: Evidence for undertreatment in women and the elderly. *Arch Intern Med* 1996; 156: 799-805

McPherson K, Wennberg JE, Hovind OB, Clifford P. Small-area variations in the use of common surgical procedures: an international comparison of New England, England, and Norway. *NEJM* 1982;307:1310-1314

Mehta, K., Fung K, , Kistler K, Chang A, Walter L. Impact of cognitive impairment on screening mammography use in older US women. *Am J of Pub Health* 2010; published ahead of print January 14, 2010.

Mezey M, Kluger M, Maislin G, Mittelman M. Life sustaining treatment decisions by spouses of patients with Alzheimer's disease. *J Am Geriatr Soc* 1996;(44)22:144–150.

Mitchell SL. Teno JM, Kiely DK, Shaffe ML, Jones RN, Prigerson, HG, Volicer L,. Givens JL, Hamel, MB. The Clinical Course of Advanced Dementia *NEJM* 2009;361:1529-1538.

Mitchell SL, Kiely DK, Hamel MB. Dying with advanced dementia in a nursing home. *Arch of Int Med* 2004;164:321-326.

Monette J, Gurwitz JH, Rochon PA, Avorn J. Physician attitudes concerning warfarin for stroke prevention in atrial fibrillation: results of a survey of long-term care practitioners. *J Am Geriatr Soc*. 1997; 45: 1060–1065.

Morris JN, Fries BE, Mehr, Cat DR, Hawes H, Phillips C, Mor V, Lipsitz, LA. . Cognitive Performance Scale. *Journal of Gerontology* 1994 49(4):M174-M182

National Comprehensive Cancer Network (NCCN) and American Cancer Society (ACS). Advanced Cancer and Palliative Care: Treatment Guidelines for Patients. 2003.

Nelder, J. A., Wedderburn, R. W.M. (1972). Generalized linear models. Journal of the Royal Statistical Society, Series A 135, 370–384.

Nelson H, Nelson, J. The Patient in the Family: An Ethics of Medicine and Families Routledge, New York, NY, 1995.

Nicholson A, Andrew I, Etherington R, Gamlim R, Lovel T. Futile and inappropriate prescribing: An assessment of the issue in a series of patents admitted to a specialist palliative care unit. *Int J of Pharm Prac* 2001;9:R72.

Opotowsky AR, Williams JM, Cannon CP. Gender differences in aspirin use among adults with coronary heart disease in the United States. *J Gen Intern Med* 2007;22(1):55–61.

Ory MG, Hoffman RR, Yee JL. Prevalence and impact of caregiving: A detailed comparison between dementia and nondementia caregivers. *Gerontologist* 1999;39(2):177–186.

Pan W, Connett JE. Selecting the working correlation structure in generalized estimating equations with application to the Lung Health Study *Statistica Sinica* 2002;12: 475-490

Park KC, Forman DE, Wei JY. Utility of beta-blockade treatment for older postinfarction patients. *J Am Geriatr Soc* 1995;43:751–755.

Pearlman RA, Jonsen A. The use of quality-of-life considerations in medical decision making. *J Am Geriatr Soc* 1985;33(5):344–350.

Pearlman RA, Speer JB. Quality-of-life considerations in geriatric care. *J Am Geriatr Soc* 1983;31:113–120.

Pearlman RA, Uhlmann RF. Quality of life in elderly, chronically ill outpatients. *J Gerontol* 1991;45(2):M31–38.

Pearlman R.A. & Uhlmann R.F. Quality of life in chronic diseases: perceptions of elderly patients. *J Gerontol* 1988;43:M25-M30.

Pfeffer MA, Greaves SC, Arnold JMO, et al, for the Healing and Early Afterload Reducing Therapy (HEART) Trial Investigators. Early versus delayed angiotensin-converting enzyme inhibition therapy in acute myocardial infarction: The Healing and Early Afterload Reducing Therapy Trial. *Circulation* 1997;95:2642–2651.

Phillips LS, Branch WT, Cook CB, Doyle JP, El-Kebbi IM, Gallina DL, Miller CD, Ziemer DC, Barnes CS. Clinical inertia. *Ann Intern Med* 2001;135(9): 825-834.

Piette JD, Kerr EA. The impact of comorbid chronic conditions on diabetes care. *Diabet Care* 2006;29(3):725–731.

Plassman BL, Langa KM, Fisher GG, Heeringa SG, Weir DR, Ofstedal MB, Burke JR. Prevalence of Dementia in the United States: The Aging, Demographics, and Memory Study *Neuroepidemiology* 2007;29:125–132

Pollack CV, Gibler WB. 2000 ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: A practical summary for emergency physicians. *Ann Emerg Med* 2001;38: 229–240.

Post, S. The Moral Challenge of Alzheimer's Disease: Ethical Issues from Diagnosis to Dying. The Johns Hopkins University Press. Baltimore. 2000

Pruchno RA, Rovine MJ, Cartwright F, Wilson-Genderson M. Stability and change in patient preferences and spouse substituted judgments regarding dialysis continuation. *J Gerontol B Psychol Sci Soc Sci* 2008;63:S81–S91.

Rabins PV, Kasper JD. Measuring quality of life in dementia: Conceptual and practical issues. *Alzheimer Dis Assoc Disord* 1997;11(6):100–104.

Rabins PV, Kasper JD, Kleinman L, et al. Concepts and methods in the development of the ADRQL: An instrument for assessing health-related quality of life in persons with Alzheimer's disease. In: Albert SM, Logsdon RG (Eds). *Assessing Quality of Life in Alzheimer's Disease.* New York: Springer, pp 51–68.

Rabins P, Lyketsos C, Steele C. *Practical Dementia Care.* Oxford University Press. New York. 2006.

Raik BL, Miller FG, Fins JJ. Screening and cognitive impairment: Ethics of forgoing mammography in older women. *J Am Geriatr Soc* 2004;52:440–444.

Rango, J. The nursing home resident with dementia: clinical care, ethics and policy implications. *Ann Int Med* 1985;102:835-841.

Rathmore SS, Berger AK, Weinfurt KP, et al. Race, sex, poverty and the medical treatment of acute myocardial infarction in the elderly. *Circulation* 2000;102:642–648.

Ready RE, Ott BR. Quality of Life measures for dementia. *Health Qual Life Outcomes* 2003;1:11.

Rhymes JA, McCullough LB, Luchi RJ, Teasdale TA, Wilson NA. Withdrawing very low–burden interventions in chronically ill patients. *JAMA.* 2000;283:1061-1063

Roberts MS. Personal communication, 2009.

Rodondi N, Vittinghoff E, Cornuz J. Aspirin use for the primary prevention of coronary heart disease in older adults *Am J Med* 2005;118:1288e1–1288e9.

Rodriguez EG, Dodge HH, Birzescu MA, et al: Use of lipid-lowering drugs in older adults with and without dementia: a community-based epidemiological study. *J Am Geriatr Soc* 2002;50:1852-1856

Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1996;28:1328–1428.

Sackett DL. Evidence based medicine: what it is and what it isn't. *Br Med J* 1996(13);312:71–72.

Sackett DL, Snow JC. The magnitude of adherence and non-adherence. In: Haynes RB, Taylor DW, Sackett DL (Eds). *Adherence in Health Care*. Baltimore, MD: Johns Hopkins University Press, 1979, pp 11–22.

Sacks FM, Pfeffer MA, Moye LA, et al., for the Cholesterol and Recurrent Events Trial Investigators. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *N Engl J Med* 1996;355:1001–1009.

Sanderson BK, Mirza S, Fry R, Allison JJ, Bittner V. Secondary prevention outcomes among black and white cardiac rehabilitation patients. *Am Heart J.* 2007;153(6):980-6.

Salthouse TA. The role of memory in the age decline in digit symbol substitution performance. *J Gerontol.* 1978;33:232–238

Schmader KE, Hanlon JT, Fillenbaum GG, Huber M, Pieper C, Horner R.. Medication use patterns among demented, cognitively impaired and cognitively intact community-dwelling elderly people. *Age and Ageing* 1998;27(4):493-501.

Schneiderman LJ, Jecker NS, Honsen AR. Medical futility: Its meaning and ethical implications. *Ann Intern Med* 1990;112:949–954.

Schulz R, Martire, LM. Family caregiving in persons with dementia: Prevalence, health effects, and support strategies. American Journal of Geriatric Psychiatry, 2004;12(3): 240-249.

Semla T, Cohen D, Paveza G, et al. Drug use patterns of persons with Alzheimer's disease and related disorders living in the community. *J Am Geriatr Soc* 1993;41:408–413.

Setoguchi S, Glynn RJ, Avorn J, et al. Statins and the risk of lung, breast, and colorectal cancer in the elderly. *Circulation* 2007*;*115:27–33.

Sharkness CM, Snow DA. The patient's view of hypertension and compliance. *Am J Prev Med* 1992;8:141–146.

Silverman, M, McDowell, J, Musa D, Rodriguez E, Martin D. To treat or not to treat: Issues in decisions not to treat older persons with cognitive impairment, depression and incontinence. *J Am Geriatr Soc.* 1997;45(9): 1094–1101.

Sleath B, Thorpe J, Landerman L, et al. Medication use among black and white caregivers of older male veterans with dementia. *Am J Geriatr Pharmacother* 2004;(2)2:133–140.

Sloan FA, Trogdon JG, Curtis LH, Schulman KA. The effect of dementia on outcomes and process of care for Medicare beneficiaries admitted with acute myocardial infarction. *J Am Geriatr Soc* 2004;52:173–181.

Smedley BD, Stith AY, Nelson AR. Unequal treatment: Confronting racial and ethnic disparities in health care. Washington DC: National Academies Press, 2003.

Smith SC Jr, Blair SN, Bonow RO, Brass LM, Cerqueira MD, Dracup K, Fuster V, Gotto A, Grundy SM, Miller NH, Jacobs A, Jones D, Krauss RM, Mosca L, Ockene I, Pasternak RC, Pearson T, Pfeffer MA, Starke RD, Taubert KA. AHA/ACC Scientific Statement: AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update: A statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation.* 2001;104(13):1577-9.

Smith SR, Boyd EL, Kirking DM. Nonprescription and alternative medication use by individuals with HIV disease. *Ann Pharmacother* 1999;33:294–300.

Smith TJ, Penberthy L, Desch CE, et al. Differences in initial treatment patterns and outcomes of lung cancer in the elderly. *Lung Cancer* 1995;13:235–252.

Soumeri SB, McLaughlin TJ, Spiegelman D, et al. Adverse outcomes of underuse of beta-blockers in elderly survivors of acute myocardial infarction. *JAMA* 1997;277:115–121.

Sox H. Screening for disease in older people. *J Gen Intern Med* 1998;13:424–425.

Straand J, Sandvik H. Stopping long-term drug therapy in general practice: how well do physicians and patients agree? *Fam Pract* 2001;18:597-601.

Stuckey JC, Neundorfer MM, Smyth KA. Burden and well-being: The same coin or related currency. *Gerontologist* 1996;36(5):686–693.

Sulmasy DP, Terry PB, Weisman CS, et al. The accuracy of substituted judgments in patients with terminal diagnoses. *Ann Intern Med* 1998;128:621–629.

Taylor DH, Fillenbaum GG, Ezell ME. The accuracy of Medicare claims data in identifying Alzheimer's disease. *J Clin Epidemiol* 2002;55: 929–937.

Teng EL, Chui HC. A Modified Mini-Mental State (3MS) Examination. *J of ClinPsych* 1987;48:314-318.

Teno JM, Licks S, Lynn J, Wenger N, Connors AF Jr, Phillips RS, O'Connor MA, Murphy DP, Fulkerson WJ, Desbiens, N, Knaus WA. Do advance directives provide instructions that direct care? SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment. *J Am Geri Soc*. April 1997;45(4):508-12.

Thibault GE, Mulley AG, Barnett GO, et al. Medical intensive care: Indications, interventions, and outcomes.*N Engl J Med* 1980;302:938–942.

Thomasma DC. Ethical judgments of quality of life in the care of the aged. *J Am Geriatr Soc* 1984;32(7):525–527.

Tomlinson T, Howe K, Notman M, Rossmiller D. An empirical study of proxy consent for elderly persons. *Gerontologist* 1999;30:54–63.

Truog RD, Frader JE, Brett AS. The problem with futility. Reprinted in: *Health Care Ethics: Critical Issues for the 21st Century.* Gaithersburg, MD: Aspen Publishers, 1998, pp 323–329.

Tunis S. Reflections on science, judgment, and value in evidence-based decision making: A conversation with David Eddy. *Health Affairs* Published online June 19, 2007.

Ubachs-Moust J, Houtepen R, Vos R, ter Meulen R. Value judgments in the decision-making process for the elderly patient. *J Med Ethics* 2008;34:863–868.

Uhlmann RF, Pearlman RA. Perceived quality of life and preferences for life-sustaining treatment in older adults. *Arch Intern Med* 1991;151(3):495–497.

US Census Bureau accessed at http://www.census.gov/index.html accessed on August 30, 2009.

Vaccarino V, Rathore SS, Wenger NK, et al. Sex and race differences in the management of acute myocardial infarction, 1994 through 2002. *N Engl J Med* 2005;353:671–682.

Valcour VG, Masaki KH, Curb JD, et al. The detection of dementia in the primary care setting. *Arch Int Med* 2000;160:2964-2968.

Van der Steen JT, Ooms M, Ader H. Withholding antibiotic treatment in pneumonia patients with dementia. *Arch Intern Med* 2002;162:1753–1760.

Veterans Administration, Department of Defense. VA/DoD clinical practice guideline for diagnosis and management of hypertension in the primary care setting. Washington (DC): Veterans Administration, Department of Defense; 2004 Aug. 99 p.

Vrakking AM, van der Heide A, van Delden JJM, et al. Medical decision-making for seriously ill non-elderly and elderly patients. *Health Policy* 2005;75:40–48.

Walker MD, Salek SS, Bayer AJ. A review of quality of life in Alzheimer's disease. Part 1: issues in assessing disease impact. *Pharmacoeconomics.* 1998;14 (5): 499-530.

Walter JJ, Shanon TA. *Quality of Life: The New Medical Dilemma.* New York: Paulist Press, 1990.

Walter LC, Eng C, Covinsky KE. Screening mammography for frail older women .*J Clin Oncol* 2008;26:2482-2488.

Walter LC, Covinsky KE. Cancer screening in elderly patients: A Framework for individualized decision making. *JAMA* 2001;285:2750–2756.

Walter, LC, Davidowitz NP, Heineken, Covinsky KE. Pitfalls of Converting Practice Guidelines into Quality Measures. *JAMA* 2004;291:2466-2470.

Weiner M, Powe N, Weller WE, Shaffer TJ, Anderson GF. Alzheimer's disease under managed care: implications from Medicare utilization and expenditure patterns. *JAGS* 1998;46:762-770

Wennberg JE, Fisher ES, Stukel TA, Sharp SM. Use of Medicare claims data to monitor provider-specific performance among patients with severe chronic illness. *Health Affairs* web exclusive, 7 Oct 2004; 10.1377/hlthaff.var.5.

Wennberg J. Professional uncertainty and the problem of supplier-induced demand. *Soc Sci Med* 1982;16:811–824.

Wennberg JE. Practice variations and health care reform: Connecting the dots. *Health Affairs* web exclusive, 7 Oct 2004; 10.1377/hlthaff.var.140.

Wechsler D. (1981) WAIS-R manual. Psychological Corporation, New York, NY.

Whittle J, Conigliaro J, Good CB, Lofgren RP. Racial differences in the use of invasive cardiovascular procedures in the Department of Veterans Affairs medical system. *N Engl J Med* 1993;329:621–627.

Whittle J, Conigliaro J, Good CB, Lofgren RP. Race and sex differences in rates of invasive cardiac procedures in US hospitals. *Arch Intern Med.* 2003;163(4):461-6.

Wilchesky M, Tamblyn R, Huang A. Validation of diagnostic codes within medical services claims. *J Clin Epidemiol* 2004;57:131–141.

Wolf-Klein G, Pekmezaris R, Chin L, Weiner J. Conceptualizing Alzheimer's disease as a terminal medical illness. *Am J Hosp Palliat Care* 2007;24(1):77–82.

Woolf SH. Practice guidelines: A new reality in medicine. III. Impact on patient care. *Arch Intern Med* 1993;153:2646–2655.

Xie J, Brayne C, Matthews FE. Survival times in people with dementia: analysis from population based cohort study with 14 year follow-up .*BMJ* 2008; 336: 258-262.

Yusuf S, Peto R, Lewis J, et al. Beta blockade during and after myocardial infarction: An overview of the randomized trials. *Prog Cardiovasc Dis* 1985;27:335–371.

Yusuf S, Sleight P, Poge J, et al. Effects of an angiotensin converting-enzyme inhibitor ramipril, on cardiovascular events in high risk patients. *N Engl J Med* 2000;342:145–153.

Zeger, SL, Liang, KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986;42:121–130.

Zeger, SL, Liang, KY, Albert, PS. Models for longitudinal data: A generalized estimating equations approach. *Biometrics* 1988;44:1049–1060.

Zimmerman, SI, Magaziner, J. Methodological issues in measuring the functional status of cognitively impaired nursing home residents: the use of proxies and performance-based measures. *Alzheimer's Disease and Associated Disorders: An International Journal.* 2008; 8: S281-S290.

Zorn CJW. Generalized estimating equation models for correlated data: A review with applications. *Am J of Political Science.* 2001;45:470-490.

Zuckerman IH, Ryder PT, Simoni-Wastila L, et al. Racial and ethnic disparities in the treatment of dementia among Medicare beneficiaries. *J Gerontol B Psychol Sci Soc Sci* 2008;(63)5:S328–S333.

Zuanetti C, Latini R, Maggioni A, Franzosi M, Santoro L, Tognoni G. Effect of ACE Inhibitors on mortality in diabetic patients with acute myocardial infarction *Circulation* 1997;96:4239-4245.