FACTORS MODERATING THE ASSOCIATION BETWEEN MULTIPLE RATING SOURCES OF GERIATRIC DEPRESSION: SELF, INFORMANT, AND PHYSICIAN

by

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A thesis submitted in partial fulfillment
of the requirements for the degree

of

MASTER OF SCIENCE

in

Psychology

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UTAH STATE UNIVERSITY
Logan, Utah

2011

ABSTRACT

Factors Moderating the Association between Multiple Rating Sources of Geriatric Depression: Self, Informant, and Physician

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Utah State University, 2011

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Late-life depression is a major public health concern, associated with poor health outcomes, including doubling of dementia risk. Psychiatric evaluation is impractical in large epidemiological studies, which instead typically rely on self/informant reports, which are subject to various biases (stigma, recall). Few studies have addressed level of agreement between sources. This study examined associations between these sources and assessed whether subject and informant variables moderated these associations. In a population-based study of dementia in Cache County, Utah (2002-5), 1,480 subjects completed an in-depth clinical assessment (CA). Major depression was assessed via the self-report Patient Health Questionnaire-9 (PHQ-9) and informant-rated Neuropsychiatric Inventory (NPI-CA). One hundred forty-eight subjects with cognitive impairment also completed a psychiatrist's examination, including the self-report Geriatric Depression Scale (GDS), the informant-rated NPI (NPI-MD), and the physician's clinical rating

(PCR). Bivariate correlations were modest: NPI-CA versus PHQ-9 (r = .26), NPI-MD versus GDS (r = .20), GDS versus PCR (r = .22), NPI-MD versus PCR (r = .45). Kappa statistics and logistic regression models indicated that the NPI-CA predicted the PHQ-9 moderately (κ =.08, p <.001; OR = 3.1, 95% CI: 1.5 to 6.1). Results also indicated that the GDS did not significantly predict the PCR (κ = .10, p > .05; 95% CI: 0.7 to 11.2) nor the NPI-MD (κ =.01, p > .05; 95% CI: 0.6 to 6.3), and that the NPI-MD predicted the PCR moderately well (κ = .35, p < .001; OR= 11.1, 95% CI: 2.6 to 48.3). CA-NPI predicted the PHQ-9 for cognitively normal subjects (κ =.13, p < .001; OR = 10.1, 95% CI: 1.9 to 52.6) but not for subjects with mild impairment (κ =.01, p > .05; 95% CI: 0.4 to 4.3) nor dementia (κ = .14, p > .05; 95% CI: 0.9 to 7.8). No other variables moderated these associations. Results suggest the importance of cognitive assessment when measuring late-life depression via self-report.

(129 pages)

ACKNOWLEDGMENTS

I would like to thank Dr. Kathleen Welsch-Bohmer and other Cache County Study on Memory Health and Aging investigators for making available to me the data set for this thesis. I would especially like to thank my major professor, Dr. Maria Norton, and my other committee members, Dr. JoAnn Tschanz and Dr. Scott DeBerard, for their support and guidance.

In addition, I give thanks to my colleagues for their advice and guidance, and to my friends and family for their support and encouragement throughout this project.

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CHAPTER I

INTRODUCTION

Depression is common among the elderly, with prevalence rates among this group (defined in most studies as persons over age 65) ranging from 86% to 9.4% for major and 3.1% to 12.9% for minor depression (Djernes, 2006). This is particularly concerning given finding that the proportion of elderly persons in the United States is increasing. For instance, the U.S. Census Bureau projected that by the year 2030, one out of five persons will be over the age of 65 (U.S. Census Bureau, 2008). Much research has been devoted to late-life depression. Late-life depression is associated with increased risk for illnesses such as heart disease (Williams et al., 2002), decreased immune functioning (McGuire, Kiecolt-Glaser, & Glaser, 2002), and osteoporosis (Robbins et al., 2001), and is associated with increased mortality after acute myocardial infarction (Carney et al., 2003). Several studies, including a review by Jorm (2001), have found that depression increases the risk for dementia (Dal Forno et al., 2005; Dotson, Resnick, & Zonderman, 2008; Fuhrer, Dufouil, & Dartigues, 2003; Hebert et al., 2000; Kessing & Andersen, 2004; Sachs-Ericsson, Joiner, Plant, & Blazer, 2005; Shim & Yang, 2006; Steffens et al., 2004), while some have found that it does not increase this risk (Chen, Ganguli, Mulsant, & DeKosky, 1999; Dufouil, Fuhrer, Dartigues, & Alperovitch, 1996; Henderson et al., 1997; Vinkers, Gussekloo, Stek, Westendorp, & Van der Mast, 2004). Quality of life is also often impaired in late-life depression sufferers. In a recent study by Doraiswamy, Khan, Donahue, and Richard (2002), recurrent sufferers of late-life major depression, as measured by the Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960)

scored worse than a normative sample on five out of eight dimensions of the Medical Outcomes Short Form-36 Health Survey (SF-36; Ware, 1993) including general health perception, mental health, emotional functioning, social functioning, and vitality. Late-life depression also may contribute to withdrawal, apathy, lack of vigor (Adams, 2001), fatigue, and some types of insomnia (Christensen et al., 1999), and increases the risk of suicide (Conwell, Duberstein, & Caine, 2002; Minino, Arias, Kochanek, Murphy, & Smith, 2002).

Before late-life depression can be studied or treated, it has to be accurately diagnosed. However, several factors impede an accurate diagnosis of depression. Older adults (and their family members) may consider depressed mood as a normal part of aging, especially in the presence of stressful life events or chronic stressors (Allen, Walker, Shergill, D'Ath, & Katona, 1998). Elderly users of some medications such as antihypertensives may also experience depressed mood as a side effect of the medication (Ried, Tueth, Handberg, Kupfer, & Pepine, 2005) and if such side effects were anticipated, the depressed mood may likewise be considered normal "background" experience and nothing noteworthy and thus, would go unreported.

The stigma associated with mental illness may well inhibit an accurate diagnosis, especially among the elderly. A study by Allen and colleagues (1998) found that older adults were more likely than younger adults to have negative beliefs about depression, including the belief that depression mainly affects women and that it is unlikely to affect elderly persons. It also found that elderly persons were more likely to report that they would approach no one for help if they suffered from depression.

Cultural beliefs among the elderly also inhibit accurate diagnosis. A study by Switzer, Wittink, Karsch, and Barg (2006) found that when elderly participants were asked questions about how one should treat depression, most participants' (83%) responses included themes involving personal responsibility, often using methaphors involving effortful movement—"(pull) yourself up by the bootstraps," "you gotta have the willpower to dig yourself out," "I get up and go out and do something, take care of it." If elderly persons view treatment of depression as primarily or exclusively their own responsibility, they may be reluctant to disclose depression to physicians or other professionals. The article also noted that most elderly persons were raised in a culture where they had to pay up front for medical and other services, due to lack of Medicare and Medicaid programs, and lack of health insurance offered as an employee benefit. Further, most medical insurance policies have greatly reduced coverage for mental health claims, when compared to physical ailments. This not only reduces financial incentive for disclosure of depression, but the disparity in coverage may send a subtle message that mental health issues are less socially acceptable. This may engender a habit of seeking services for only the most urgent conditions.

Dementia may also lead to an inaccurate diagnosis of late-life depression (Burt & Zembar, 1995; Manthorpe & Iliffe, 2006). In clinical practice and in epidemiological studies of cognitive impairment, in order to render an accurate diagnosis of depression, cognitive impairment needs to be taken into account. Likewise, when the main objective is to render an accurate diagnosis for dementia, clinicians need to consider the presence of depression. An accurate assessment of both cognitive status and depression help to

determine whether depression is the sole causal factor explaining impairment or whether depression is part of the symptom profile of an individual with dementia. However, the presence of cognitive impairment may affect depression reporting in some individuals. For instance, some studies have found that elderly persons are not aware of their depressive mood. This impaired insight seems to be linked to dementia. Several (Ott & Fogel, 1992; Ott, Lafleche, Whelihan, & Buongiorno, 1996) but not all (Reed, Jagust, & Coulter, 1993) studies have found a link between dementia severity and impaired awareness of depression. This impaired awareness of depression may render depression reports invalid, unless auxiliary informant report is available.

However, informant reports which are often used in clinical practice and in epidemiological studies, suffer from some of the same confounders. They too may be influenced by social stigma, and they too may experience lack of awareness of depressive mood. In addition, informant reports can be influenced by the degree to which informants are familiar with the subject, which is affected by the type of relationship to the subject, the strength of that relationship, and geographic proximity to the subject.

Nevertheless, obtaining depression data from multiple sources is often preferable to reliance on self-report alone. In epidemiological studies, where feasible, self-reports and informant reports are often supplemented by physician evaluations, since physicians can rely not only on written assessments but also on their own clinical judgment in meeting with the subject. However, physician evaluations, considered by many to be the "gold standard" in assessment of psychiatric conditions, are not economically feasible in large-scale epidemiological studies. In such studies where thousands of participants must

be evaluated, reliance on either self-report or informant report is common. While either source of data alone is subject to the greatest risk of bias, a triangulation approach of collecting data from multiple sources—subject and informant(s) may reduce this bias.

A small number of studies have addressed the strength of association between self-report, informant report, and physician report. For instance, a study by Teri and Wagner (1991) revealed that patients had lower depression ratings than caregivers (mean patient =5.0 versus mean caregiver = 7.6, $t(70) = 4.53$, $p < .0001$, Cohen's $d = 0.38$) and clinicians (mean patient =5.0 versus mean clinician = 8.2, $t[69] = 6.20$, $p < .0001$, Cohen's $d = 0.46$, respectively), and that caregivers had lower depression ratings than clinicians $t(67) = 2.19$, $p < .05$, Cohen's $d = 0.09$. Few other studies addressed the extent to which degree of cognitive impairment of the elderly subject and background factors on the informant influence the strength of association.

Since physician evaluations of late-life depression are often not feasible in large-scale epidemiological research, it is important to assess the strength of association between subjects, informants, and clinicians, and to identify factors related to the strongest association among these sources. Studies that have examined this have found that subjects tend to be less likely to report depression than informants and clinicians. However, caution is warranted in accepting these conclusions, since these studies are sparse, and since they have all relied on clinic-based data, which may be biased toward individuals who are more likely to report symptoms.

This thesis assessed the association between subject, informant, and clinician reports of the subjects' current depression status, and assessed factors that strengthened

that association. Secondary analyses were conducted using data from a large, population-based epidemiological study of dementia, the Cache County Study on Memory, Health, and Aging, in which depression data were available from self-report, informant report, and physician examination. Such enhanced understanding of the extent of consistency between multiple reports will likely aid future community studies of geriatric depression.

CHAPTER II

LITERATURE REVIEW

Public Health Significance of Geriatric Depression

This chapter reviews the literature regarding rating sources of late-life depression. First, I demonstrate the public health impact of late-life depression by reviewing the prevalence and incidence rates of late-life depression, and by reviewing the consequences of late-life depression. I then discuss how subject characteristics, including cognitive status, stigma, beliefs among the elderly, gender, medication side-effects and medical comorbidities, and prior depression history can impact the accuracy of subjects' reports of depression. Then, I discuss the use of informants in diagnosing depression, and discuss how informant and subject characteristics can affect informant reports of depression. In addition, I discuss the use and feasibility of physician ratings of depression. Finally, I review studies that have assessed agreement between sources.

Prevalence and Incidence Rates

Major and minor depression are common among the elderly, with community-based prevalence rates ranging from 86% to 9.4% and 3.1% to 12.9%, respectively (Beekman et al., 1995; Djernes, 2006; Eaton, Kalaydjian, Scharfstein, Mezuk, & Ding, 2007; Steffens et al., 2000). This is particularly concerning given the increasing proportion of elderly persons in the United States. The Administration on Aging (2004) predicts that the number of persons aged 65 and older will increase to 39 million by 2010, to 53 million by 2020, and to 70 million by the year 2030.

Consequences of Geriatric Depression

Late-life depression can severely affect quality of life. A study by Doraiswamy and colleagues (2002) found that sufferers of late-life major depression reported decreased general health perception, mental health, emotional functioning, social functioning, and vitality. Late-life sufferers of depression are more likely to experience withdrawal, apathy, lack of vigor (Adams, 2001), hopelessness (Christensen et al., 1999), weight loss (Morley & Kraenzle, 1994), fatigue, some types of insomnia (Christensen et al., 1999), are more likely to report pain, and are more likely to have a low perception of their general health (Doraiswamy et al., 2002). Depression can also lead to suicide; depression diagnosis is present in 80% of people aged 74 or older who commit suicide (Conwell et al., 2002). This is particularly concerning given that the frequency of suicide is almost twice as high in the elderly population than in the general population (Minino et al., 2002).

Depression can also complicate cooccurring medical illness. Studies have found depression to be a risk factor for mortality after myocardial infarction (Carney et al., 2003), heart failure (among elderly women; Williams et al., 2002), and decreased immune functioning (McGuire et al., 2002). Depression among the elderly is associated with low bone-mineral density, a risk factor for osteoporosis (Robbins et al., 2001). In addition, depression is associated with poor recovery from myocardial infarction (Ladwig & Roll, 1994; Romanelli, Fauerbach, Bush, & Ziegelstein, 2002) and is associated with poor recovery from interbody cage lumbar fusion surgery (LaCaille, DeBerard, Masters, Colledge, & Bacon, 2005). Several studies, including a review by Jorm (2001), have

found that late-life depression leads to dementia (Dal Forno et al., 2005; Kessing & Andersen, 2004; Shim & Yang, 2006; Steffens et al., 2004), while other studies found no such effect (Chen et al., 1999; Dufouil et al., 1996; Henderson et al., 1997; Vinkers et al., 2004).

Subject Factors Impacting Accuracy of Depression Diagnosis

Before late-life depression can be studied, it has to be accurately diagnosed. However, several factors impede an accurate diagnosis of depression. Cognitive deficits ranging from mild cognitive impairment (MCI) to dementia may result in unawareness of depression symptoms, confounding the diagnosis of depression (McAvay, Raue, Brown, & Bruce, 2005). Additionally, individuals may be reluctant to disclose depression symptoms due to perceived negative social stigma, a misperception that depression is a normative experience in late life, or if related to medication use, may also not be reported. Each of these potential confounders is discussed in the following sections of this literature review.

Depression Diagnostic Confounders: Cognitive Impairment

Dementia as a depression diagnostic confounder. In clinical practice and in epidemiological studies of cognitive impairment, in order to render an accurate diagnosis of depression, cognitive impairment needs to be taken into account. For example, one exclusionary criterion for major depression according to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric

Association, 1994) is any medical condition that could explain the depressive symptoms (e.g., dementia). Likewise, in order to render an accurate diagnosis for cognitive disorder, clinicians need to consider the presence of depression. A fair degree of symptom overlap can exist between depression and dementia. Nondepressed and depressed dementia patients exhibit psychomotor slowing, emotional lability, weight loss, crying spells, insomnia, pessimism, inability to verbalize affective state (McGuire et al., 2002), and non-demented elderly people with depression tend to have difficulties with concentration, speed of mental processing, and executive functioning (Alexopoulos, 2005). An accurate assessment of both cognitive status and depression help to determine whether depression is the sole causal factor explaining cognitive impairment or whether depression is part of the symptom profile of an individual with dementia.

Mild cognitive impairment affects depression assessment. Level of cognitive impairment has some impact on subjects' ratings of depression. McAvay and colleagues (2005) looked at whether agreement between subject and informant ratings of symptom domains of depression, as measured by the Structured Clinical Interview for Axis I *DSM-IV* Disorders (Spitzer, Gibbon , & Williams, 1995), differed depending on level of cognitive impairment, as measured by a score out of 13 points possible of a subset of the Mini-Mental State Examination, which measures orientation to time, orientation to place, and recall of words. Lower scores on this measure indicate greater impairment. To look at agreement between sources, the authors used the Kappa statistic (Fleiss, 1981). This is a measure of interrater agreement of categorical data, and differs from traditional interrater agreement statistics in that it corrects for chance. Kappa scores of 1 indicate perfect

interrater agreement, and kappa scores ≤ 0 indicate no agreement other than that expected by chance. Landis and Koch (1977) suggested the following strength of agreement designations for Kappa values: < 0.0 = poor, 0-.20 = slight, .21 - .40 = fair, .41-.60 = moderate, .61-.80 = substantial, .81-1.0 = almost perfect. According to this statistic, agreement was lower for cognitive symptoms among subjects with more than three errors on the orientation and recall questions ($\kappa = .19$ for patients with less than three errors and $\kappa = -.10$ for patients with more than three errors). However, agreement was not lower among subjects with more than three errors for somatic symptoms ($\kappa = .30$ for patient with < 3 errors, $\kappa = .30$ for patients with 3+ errors), psychological symptoms ($\kappa = .44$ versus $\kappa = .32$), and suicidal symptoms ($\kappa = .42$ versus $\kappa = .38$).

To assess patterns of disagreement between the informant and subject, the authors used the asymmetry index (AI), a log linear model technique that involves examining the off-diagonal cell frequencies in order to assess whether informants were more likely to report symptoms than subjects. AI scores above 1.0 indicated that the informant was more likely to report symptoms, while AI scores below 1.0 indicated that the informant was less likely to report symptoms. They found that informants were more likely than patients to report psychological symptoms when patients made more than three errors (AI = 1.2 for patients with < 3 errors, AI = 1.8 for patients with 3+ errors, $p \leq .01$), and informants were less likely than patients to report suicidal symptoms when patients made less than three errors (AI = 0.3 for patients with < 3 errors, AI = 1.4 for patients with 3+ errors).

Knauper and Wittchen (1994) conducted a study assessing whether differences in

working memory capacity account for changes in self-reported depression. Differences in working memory capacity were measured by a listening span task described by Daneman and Carpenter (1980). This task assesses ability to keep verbal items in working memory while performing memory search, comprehension, and judgment tasks. Self-reported depression was assessed using the Composite International Diagnostic Interview (CIDI; Wittchen & Semler, 1991), a modified and expanded version of the Diagnostic Interview Schedule (DIS; Robins, Helzer, Ratcliff, & Seyfried, 1982). They found a negative relationship between working memory capacity and the number of physical symptoms of depression endorsed by the subject (r = -.34, df = 61, $p \leq$ .004). Using a two-step hierarchical regression analysis in which the number of physical symptoms of depression was the outcome variable, the authors found that working memory capacity remained significant after adding age to the model (Age: beta = .18, $F(1,61) = 1.82$, $p \leq .18$; Working memory: beta = -.27, $F(2,60) = 3.99$, $p \leq .05$), suggesting that the effect of working memory capacity on the number of physical symptoms of depression reported was robust to age. These findings support the conclusion that cognitive impairment may increase the number of self-reported physical symptoms of depression.

Depression Diagnostic Confounders: Perceived Negative Repercussions of Disclosure

Elderly persons may be reluctant to disclose depression because they believe that doing so may have negative repercussions. A study by Roeloffs and colleagues (2003) looked at the perceived negative effect of depression. Participants in this study were selected from clinics across several states. Forty-four percent of participants were

between the ages of 18 and 41, and 56% of participants were 41 years or older. Subjects were considered depressed if they scored positive on a five-item screening test based on the World Health Organizations Composite International Diagnostic Interview 2.1, 12 month version (CIDI-12; Wittchen & Semler, 1991) and had depressive symptoms in the past month. The authors asked participants if they thought that disclosure of "a recent history of depression" (p. 312) would negatively affect their ability to get a job, to change health insurance policies, and to maintain friendships. They also asked them similar items about disclosure of HIV, hypertension, and diabetes. A high percentage of participants expected disclosure of depression to negatively affect some aspect of their lives. Sixty-seven percent of participants expected disclosure of depression to negatively affect ability to gain employment, 59% expected it to affect their ability to obtain health insurance, and 24% expected it to negatively affect their friendships.

In bivariate analyses, older age, lower education, employment, social support, diagnosis of major depression, increased number of chronic medical conditions, and clinic location (the researchers obtained participants from clinics located in several states) were all related to the belief that depression disclosure would impact at least one area of life. Factors that were not significant in bivariate analyses included: substance misuse, hazardous drinking, and health insurance status. Using a multivariate model that controlled for socio-demographic variables and severity of illness, the authors found that the younger age group (ages 17-34) was less likely to expect disclosure to negatively affect employment than the middle age group (ages 35-59; $OR = 0.64$, $p = .035$). The oldest age group (60+ years old) did not differ from the middle age group in this area.

Age was not related to perceived effect of disclosure on health insurance or friendship. Perceived negative effect of disclosure on health insurance and friendship was higher in participants with three or more chronic medical conditions (*OR* = 1.79, *p* = .30 and *OR* = 1.50, *p* = .046, respectively). Women were more likely to perceive a negative effect of disclosure on jobs than men (*OR* = 3.70, *p* = 0.027), but a female gender by social support interaction term indicated that women with social support were less likely to perceive a negative effect of disclosure on jobs than women without social support (*OR* = 0.70, *p* = 0.039). These findings suggest that some persons, particularly the middle-aged and elderly, females, and those with a greater number of medical conditions, are more likely to report depression symptoms because of concerns about employment, health care coverage, and friendships.

The relationship between perceived negative effects of disclosure, utilization (mental health specialty visits, primary care visits for emotional reasons, primary care medical visits, and total visits) and unmet need were equivocal. Regression models using perceived negative effects of disclosure as a predictor and utilization of unmet need as a dependent variable and which adjusted for depression severity found perceived negative effects of disclosure on employment to be related to less unmet need for mental health services (*OR* = 0.24, *p* < .01). Perceived negative effects of disclosure on friendship was related to more unmet needs for mental health services (*OR* = 1.51, *p* = .037), and perceived negative effects of disclosure on health insurance was related to more medical visits (*B* = 0.89, *p* = .02) and more receipt of appropriate treatment (*OR* = 1.49, *p* = .03). There were no other statistically significant relationships between perceived negative

effects of disclosure and unmet needs/utilization variables. These findings suggest that perceived negative effects of disclosure have diverse effects on health care utilization.

Depression Diagnostic Confounders: Belief That Depression *is* a "Normal" Part of Aging

In addition to lack of awareness and stigma, older adults (and their family members) may even consider depressed mood as a normal part of aging. For instance, a study by Farrer, Leach, Griffiths, Christensen, and Jorm (2008) found that among participants aged 70 or older, fewer persons (41.5%) identified depression in a vignette depicting a 30 year old man or woman with depression than those in other age categories: 18-24 years (71.7%, $z = 4.77$, Cohen's $h = .64$), 25-39 years (70.8%, $z = 5.76$, Cohen's $h = .61$), 40-54 years (67.4%, $z = 5.0$, Cohen's $h = .53$), and 55-69 years (64.9%, $z = 4.3$, Cohen's $h = .50$).

Presence of depression may also influence the likelihood of reporting depression, although findings conflict as to whether the presence of depression makes a person more or less likely to report symptoms. Allen and colleagues (1998) found that older persons with depression, as measured by the Geriatric Depression Scale (MD-Self; Yesavage et al., 1982), were less likely than older persons without depression to report that they would approach anyone ($\chi^2 = 8.7$, Fisher's exact test $p < 0.03$), or that they would approach a spouse ($\chi^2 = 5.9$, $p < 0.03$), if suffering from depression. A study by O'Connor, Rosewarne, and Bruce (2001) found that severity of depression, as measured by the Scale for Depressive Symptoms (SDS; Henderson, Jorm, Mackinnon, & Christensen, 1993) which measures dysthymia, depressive episode, and major depressive disorder, was

independently and positively related to self-rated likelihood of reporting depression symptoms to a general practitioner (β =.143, $p < .00005$). Past psychiatric contact and female gender were also independently and positively related to self-rated likelihood of reporting depression symptoms to a general practitioner (β = .589, $p < .00005$ and β = .241, $p = .03$, respectively).

Depression Diagnostic Confounders:
Gender

Studies have found that depression is more common among females. In a review of studies assessing the prevalence of depression among older persons, Djernes and colleagues (2006) found that older females were more likely to have depression than older males (odd ratios: 3.4 to 1.3). However, several lines of evidence suggest that this increased prevalence may be due in part to reporting artifact. Hinton, Zweifach, Oishi, Tang, and Unutzer (2006) found, for example, that older males with major depression or dysthymia, as measured by the Structured Clinical Interview for DSM-IV (SCID; Spitzer, Williams, Gibbon, & First, 1992), were less likely to seek treatment than older females with major depression or dysthymia. In a series of multiple regression models that controlled for marital status, minority status, presence of two or more prior depression episodes, presence of suicidal thoughts, presence of cognitive impairment (as determined by a screening question), depression score, and site from which the participant was recruited, the researchers found that men were less likely to use any antidepressant in the previous three months ($OR = 1.42$, $p = 0.0038$), to receive any depression care in the previous three months ($OR = 1.43$, $p = 0.0031$), to receive any depression care throughout

their lifetime ($OR = 1.74$, $p < 0.0001$), or to receive potentially effective depression treatment, defined as at least four sessions of psychotherapy or at least two months of antidepressant usage ($OR = 1.69$, $p = 0.0002$). Older males may avoid treatment because they are reluctant to admit that they have depression symptoms.

Estimates of gender disparities in depression may also be distorted because of different symptom patterns among males and females. For instance, Hinton and colleagues (2006) found that depressed older men were less likely than depressed older women to report that they felt depressed or down (men: 39% versus women: 47%, $\chi^2 = 21.24$, $p < 0.001$), that they had lost interest in the things they enjoyed (men: 37% versus women: 42%, $\chi^2 = 7.14$, $p = 0.008$), that they felt fatigued (men: 62% versus women: 67%, $\chi^2 = 7.49$, p = 0.008), and that they had appetite problems (men: 34% versus women: 41%, $\chi^2 = 14.36$, $p < 0.001$). Men are also more likely than women to commit suicide. A study by the Centers for Disease Control and Prevention (Minino et al., 2002) found that among persons of all ages suicide rates were four times higher among men than among women (18.1 per 100,000 in men versus 4.0 per 100,000 in women). Some authors have argued that current depression instruments reflect symptom patterns more closely associated with the female gender. If this is so, current depression instruments may underestimate depression among males (Möller-Leimkühler, 2002).

Hinton and colleagues (2006) also found that men express depression differently. In semistructured interviews of primary care physicians, depression care managers (nine nurses and two psychologists), and research assistants, respondents expressed a belief that men were less likely to express the emotional aspects of depression. For example,

one physician said, “Women in general are much more likely to present with mood symptoms saying they are feeling depressed or feeling anxious or nervous. I think men in general, especially older men, are much less likely to mention those red flag kind of words.” Respondents had various explanations for this discrepancy. Some stated that men did not express the emotional aspects of depression because they do not recognize them, while other respondents stated that they purposefully tried to hide them from others.

In addition, some respondents stated that men were less willing to accept a depression diagnosis. For example, one primary care physician stated, “They [men] just do not go with the labels. They’ll say, no I’m not sleeping well, I have aches and pains. It seems to be a leap for them to accept depression treatment for that. The men recognize the symptoms, but they still do not think it is them.” The study found that this reluctance to admit depression may be due to traditional conceptions of masculinity. Some respondents described a subgroup of men who believed that men should be self-sufficient, stoic, and tough. These men may be reluctant to express or report symptoms of depression such as worthlessness, helplessness, and sadness for fear of seeming unmanly.

Depression Diagnostic Confounders: Medication Side-Effects and Medical Comorbidities

Comorbid medical conditions may also confound the diagnosis of depression among the elderly when using self-report or informant report (Alexopoulos, 2005). Depression can be a side effect of some medications, including beta-blockers (Alexopoulos, 2005; D.C. Steffens, personal communication, March 30, 2009) and some steroids (Brown & Suppes, 1998; D.C. Steffens, personal communication, March 30,

2009). Depression can also be a side effect of interferon (Zdilar, Franco-Bronson, Buchler, Locala, & Younossi, 2000; D.C. Steffens, personal communication, March 30, 2009), although this drug is rarely used. If such side effects were anticipated, the depressed mood may likewise be considered normal 'background' experience and nothing noteworthy.

As noted by several authors (Alexopoulos et al., 2002; McAvay et al., 2005) elderly patients are more likely to report symptoms of medical illness and to omit symptoms of mental illness when communicating with their physicians, which makes a depression diagnosis less likely. This is likely to occur in patients with medical conditions related to depression. These include vascular conditions such as heart attack (Alexopoulos, 2005), stroke (Yamaguchi, Kobayashi, Koide, & Tsunematsu, 1992), hypertension (Jonas, Franks, & Ingram, 1997), type II diabetes (Anderson, Freedland, Clouse, & Lustman, 2001), and hypercholesterolemia (Van Melle et al., 2006), as well as other conditions such as viral infection, endocrinopathy, malignant disease, and metabolic disorders (Alexopoulos, 2005). The symptoms of some medical conditions mimic the symptoms of depression. For instance, the symptoms of apathetic delirium include reduced speech, withdrawal, and nonspecific dysphoria (Armstrong, Cozza, & Watanabe, 1997). Some elderly persons deny having depressed mood but report a lack of feeling or mood or a lack of interest in normally pleasurable activities. This tendency of elderly persons to omit the affective symptoms of depression has been described as "depression without sadness" (Gallo & Rabins, 1999).

Depression Diagnostic Confounder: Prior Depression History

Depression incidence is higher among persons with a prior history of depression. A study by Norton and colleagues (2006b) found that incidence of major depression per 1,000 person years, as measured by the Diagnostic Interview Schedule (DIS), was greater for participants with a prior minor depressive episode (23.0) than it was for participants without a prior minor depressive episode (8.32). A study by Murphy and colleagues (2002) was consistent with this finding. They found that the incidence of major depression per 1,000 person years, as measured by the DIS, was much higher for participants with a prior history of dysthymic disorder (210.5), than it was for participants in a reference category (4.0). This relationship is likely due to the chronic nature of depression. However, it may also be a reporting artifact; the relationship between incidence and prior history may indicate a greater willingness to report symptoms among some persons.

Informant-based Report of Geriatric Depression

Often, collateral informants are also queried about depression symptoms of older adults, given that they are typically used as confidantes and provide an important additional perspective. In a mixed methods study of current and recent sufferers of late-life depression, Piercy, Norton, and Cloward (2007) found that older adults' primary source for emotional support for depression was close family members. In fact, most expressed reluctance to seek emotional help from or disclose depressive symptoms to anyone but close family members. This suggests the need for a more family-systems

approach in both clinical practice and epidemiologic studies, in which information about the older adult's depressive symptoms is obtained from both self-report and through family members. However, informant reports used in clinical practice and in epidemiological studies suffer from some of the same confounders; they too may be influenced by perceived social stigma, and they too may experience lack of awareness of depressive mood.

Various types of informants can be seen in the research literature on geriatric depression. McAvay and colleagues (2005) used spouses, children-in-law or children, siblings, friends, and "other relatives" as informants of depression. In other studies of informant reports of depression informants were described simply as "caregivers" (Teri & Wagner, 1991). A study by Castle (2005) on informant reports of patient care satisfaction used "family members." Some studies of informant reports of depression used employees as informants (Bourgeois, Dijkstra, & Hickey, 2005; McAvay et al., 2005). A study by Ott and colleagues (1996) on informant reports of memory and functional decline also used employees as informants.

As subjects get older, the availability of the spouse as the informant decreases due to mortality. Because of this, researchers often use adult children, friends, and other more distant relatives as informants. These informants are often less knowledgeable of the subject's affective state than the spouse. In addition, informant reports of the subject's affective state can be influenced by other factors, such as the number of years the informant has known the subject, and frequency of contact with the subject, since these factors affect the amount of interaction between the informant and the subject.

Clinician Evaluation of Depression

Because of these limitations, self-reports and informant reports are often supplemented in research studies by physician evaluations, since physicians can rely not only on written assessments but also on follow-up questioning, observations, and their own clinical judgment in meeting with the subject. However, physician evaluations, considered by many to be the "gold standard" in assessment of psychiatric conditions, are simply not economically feasible in large-scale epidemiological studies. In such studies where thousands of participants must be evaluated, reliance on either self-report or informant report is common. While either source of data alone is subject to the greatest risk of bias, a triangulation approach of collecting data from multiple sources (subject and informant) reduces this bias.

Several instruments can be used to assess late-life depression. The Patient Health Questionaire-9 (PHQ-9; Kroenke, Spitzer, & Williams, 2001) is a nine-item depression instrument that can be self-administered. This instrument uses a symptom checklist to diagnose major depression as well as subthreshold depression, which it calls "other depressive disorder." The Geriatric Depression Scale (Yesavage et al., 1982) is a 30-item self-report measure of depression specifically designed for the elderly. Like the PHQ-9, the GDS uses a symptom checklist to diagnose depression. Informant report may come from an instrument such as the Neuropsychiatric Inventory (NPI; Cummings et al., 1994). The NPI is an informant-based assessment and is specifically designed for persons with dementia. The NPI uses semi-structured interviews to measure ten behavioral domains, including depression/dysphoria. Like the GDS and PHQ-9, the NPI uses a symptom

checklist to assess depression. The NPI also asks about the frequency and severity of depression symptoms.

Association of Depression Reports between Multiple Sources

There have been very few published studies that have addressed the extent of association between self-report, informant report, and clinician reports of geriatric depression. Each of these studies and their limitations are summarized below.

Self-Report versus Informant-Report of Depression

McAvay and colleagues (2005) looked at the association between patient and informant reports of depression. Patients in this study were recruited from medical home care centers. Mean patient age was 78 years (range 65-100). In a study of 539 generally cognitively normal patients from medical home care, 430 were able to nominate "a family member or close friend" (p. 509) to be an informant. Informants in this study included spouses (40.6%), children or children-in-law (36.9%), 17 siblings or siblings-in-law (4.8%), other relatives (5.4%), friends (11.8%), and 2 paid employees (0.6%). Most of the informants were female (73%). Patients and informants were interviewed using the Structured Clinical Interview for Axis I *DSM-IV* Disorders (Spitzer et al., 1995). The authors postulated that the association between sources of information would depend on the type of depression symptomatology, as well as level of cognitive impairment, informant age, patient and informant gender, and whether or not the informant had daily contact with the patient. Types of depression symptomatology included somatic

symptoms (decreased appetite or weight loss, increased appetite or weight gain, psychomotor agitation or psychomotor retardation, insomnia or hypersomnia, fatigue or loss of energy), cognitive symptoms (indecisiveness or diminished ability to concentrate or think), psychological symptoms (diminished interest or pleasure, depressed mood, worthlessness, inappropriate guilt), and suicidal symptoms (thoughts of death, suicidal ideation). To compute scores for each symptom domain, the authors counted the number of symptoms endorsed in each (somatic: 0-3+, cognitive: 0-1, psychological: 0-2+, suicidal: 0-1). Cognitive functioning was assessed using a score out of 13 total points possible of a subset of the Mini-Mental State Examination which measured orientation to time, orientation to place, and recall of words (MMSI; Folstein, Folstein, & McHugh, 1975).

In general, agreement was fair or poor in all four depression domains. It was found that informants were more likely than patients to report psychological and cognitive symptoms (asymmetry index [AI] =1.4, $p \leq .001$, and AI = 1.7, $p \leq .05$, respectively; $\kappa = .41$ and $\kappa = .09$, respectively) and that informants were less likely than patients to report suicidal symptoms (AI =.52, $p \leq .10$, $\kappa = .41$). Disagreement was poor for the somatic domain ($\kappa = .31$, no AI reported) and did not follow a definite pattern.

Level of cognitive impairment had some impact on agreement. Kappa showed mostly agreement. Kappa was lower in the cognitive domain among subjects with more errors on the orientation and recall questions ($\kappa = .19$ for patients with less than three errors and $\kappa = -.10$ for patients with more than three errors). However, kappa was not lower among subjects with more errors in the somatic ($\kappa = .30$ for patient with < 3 errors,

κ = .30 for patients with 3+ errors), psychological (κ = .44 for patient with < 3 errors, κ = .32 for patients with 3+ errors), and suicidal domains (κ = .42 for patient with < 3 errors, κ = .38 for patients with 3+ errors). Less agreement was shown in the AI. Informants were more likely than patients to report psychological symptoms when patients made more than three errors (AI = 1.2 for patients with <3 errors, AI = 1.8 for patients with 3+ errors, $p \leq .01$), and were less likely than patients to report suicidal symptoms when patients made less than three errors (AI = 0.3 for patients with < 3 errors, AI = 1.4 for patients with 3+ errors, $p \leq .05$).

Informant age had some effect on agreement. It did not affect kappa agreement on any of the domains. However, the AI showed that agreement was affected by informant age. It was found that younger informants (23 to 64 years of age) were more likely than older informants (65 to 95 years of age) to report more psychological symptoms than patients (AI = 1.6 versus 1.1, respectively), and to report more cognitive symptoms than patients (AI = 3.7 versus 0.8, respectively). AI did not vary by age for the somatic and suicidal domains.

Although the researchers found that patient gender, informant gender, and frequency of contact with the patient affected agreement, they were unable to make any certain conclusions about the effects of these factors because of the high correlations between them. For instance, the authors found that 90% of male patients used female informants, whereas only 59% of female patients had female informants. Because of this, the authors could not conclude whether differences in AI among male and female patients were due to patient gender or to informant gender.

Snow and colleagues (2005) found that discrepancy between patient reports and informant and clinician reports of depression were not due to dementia per se, but to patient awareness of dementia deficits. In this study, researchers conducted two hierarchical regression models. In one model, severity of cognitive impairment (as measured by the cognitive subscale of the Alzheimer's Disease Assessment Scale), physical illness, functional status, caregiver burden, clinician reports of depression (Cornell Scale for Depression in Dementia), and awareness of dementia were entered as predictors, and patient/informant depression discrepancy scores (difference between the summed informant rated Geriatric Depression Scale scores and the summed patient-rated GDS scores) were entered as the dependent variable. Informants in this study were relatives, friends, and caregivers and had at least four hours of contact a week with the patient each week. Although the authors did not include gender in their analyses, it appeared to be an important factor. Demographic information reported in the study revealed that females may have been less likely to be diagnosed with only depression; whereas the control, dementia only, and depression and dementia groups were 52%, 42%, and 45% female, respectively, the depression only group was only 23% female.

The authors found that among patients with and without a previous diagnosis of dementia, awareness of dementia was the only factor that predicted the discrepancy between patient and informant depression scores (dementia sample: $F[7,65] = 3.63$, informant-patient DDS discrepancy $\beta = 0.60$, $p < .005$; nondementia sample: $F[7,54] = 4.08$, informant-patient DDS discrepancy $\beta = 0.57$, $p < .001$). A similar model used severity of cognitive impairment, physical illness, functional status, informant-rated GDS

scores, and awareness of dementia (as measured by the patient-clinician discrepancy score on the DDS) as predictors and patient-clinician depression discrepancy scores (difference between the summed clinician-rated Cornell Scale for Depression in Dementia scores and the summed patient-rated GDS scores) as the dependent variable. Findings were similar to those in the first model; among patients with a previous diagnosis of dementia, awareness of dementia deficits was the only factor that predicted the discrepancy between patient and clinician depression scores, $F(6,54) = 2.92$, informant-patient DDS discrepancy $\beta = 0.32$, $p < .05$.

The authors also found, in turn, that awareness of dementia deficits depends on dementia diagnosis. Patient-informant discrepancies on the DDS indicated that patients previously diagnosed as having dementia or as having both dementia and depression were significantly more likely to report fewer dementia symptoms than were controls or patients previously diagnosed with depression only (mean discrepancies $\pm$ *SD*: controls; -0.54 $\pm$ 0.56, depression only; -0.54 $\pm$ 0.81, dementia only; 0.43 $\pm$ 0.99, depression and dementia; 0.26 $\pm$ 1.33; scores above 0 indicated that the informant rated depression higher, while scores below 0 indicated that the patient rated depression higher; controls versus dementia only: $p < .01$, controls versus depression and dementia: $p < .05$, depression only versus dementia only: $p < .01$, depression only versus depression and dementia: $p < .05$). Patient-clinician discrepancies on the DDS revealed similar findings. Patients previously diagnosed as having dementia or having both dementia and depression were significantly more likely to report fewer dementia symptoms than were patients previously diagnosed with only depression (mean discrepancies: depression only;

-1.23, dementia only; 0.51, depression and dementia; 0.08; depression only versus dementia only: $p < .001$, depression only versus depression and dementia: $p < .01$).

Self-Report Versus Physician Rating of Depression

Ott and Fogel (1992) looked at the association between self-report, caregiver report, and clinician report of depression. In this study the authors used the Geriatric Depression Scale (Yesavage et al., 1982) to assess self-reports of depression, the HAM-D (Hamilton, 1960) to measure caregiver reports of depression, and the Cornell Depression Scale for Depression in Dementia (Alexopoulos, Abrams, Young, & Shamoian, 1988) to measure clinician reports of depression. The study also looked at how awareness of dementia affected the strength of association between rating sources. Researchers assessed impaired insight of dementia using a self-report questionnaire that asked if patients had (a) awareness of the situation, (i.e., reason for the office visit), (b) awareness of memory impairment, (c) awareness of impairment in activities of daily living, and (d) awareness of progression of deficit. Each question was scored on a 0-2 scale, with a total possible range of 0-8. Higher scores on this measure indicated less insight. Dementia severity was also assessed in order to ascertain its effect on the strength of association. Three scales were used for this: The Clinical Dementia Rating Scale (Morris, 1993) possible range 0-3, higher scores indicate greater impairment), the MMSE (range 0-30, lower scores indicate greater impairment), and the brief Orientation-Memory-Concentration Test (Katzman et al., 1983) possible range 0-28, higher scores indicate greater impairment). 41 of the 50 participants in the study obtained MMSE scores ≤ 26.

Mean Clinical Dementia Rating Scale score was 1.1 (*SD* = 0.7), mean MMSE score was 20.3 (*SD* = 7.5), and mean OMC score was 13.7 (*SD* = 8.2), indicating a range of cognitive impairment. Of the 50 participants, 23 were male, and 27 were female. Since caregiver depression could affect ratings of patient depression, researchers also administered the GDS to caregivers.

Researchers found that caregiver depression did not affect ratings of patient depression and that dementia and impaired insight of dementia decreased the association between patient and clinician reports of patient depression. GDS scores of caregiver depression correlated poorly with clinician-rated COR scores and caregiver-rated HAM-D scores (HAM-D: $r = 0.202$, $p = 0.245$; COR: $r = 0.266$, $p = 0.123$), indicating that caregiver depression did not affect caregiver ratings of patient depression. The HAM-D and COR correlated well ($r = 0.92$, $p < 0.0005$), indicating congruence between caregiver and clinician reports. Insight and cognitive impairment were strongly related (insight and MMSE: $r = -0.67$, $p < 0.005$; insight and OMC; $r = 0.64$, $p < 0.005$). GDS and COR scores were only moderately associated ($r = 0.40$, $p = .0004$). This correlation was even lower among patients with MMSE scores less than 22 and insight scores greater than two ($r = 0.15$, p value not reported). In addition, a multivariate analysis using MMSE score, clinical dementia rating, diagnosis of AD, insight score, history of depression, age, sex, and education as predictor variables revealed clinical dementia ratings and insight scores to be the only significant predictors of GDS-COR discrepancy scores (clinical dementia ratings: coefficient = -3.12, t = -2.38, $p = 0.02$; insight score: coefficient = -1.39, $t = -4.25$, $p < 0.0005$). MMSE scores approached significance (coefficient = -0.16,

t = -1.21, p = 0.23).

Self- Versus Informant- Versus Clinician Ratings

Teri and Wagner looked at the association between AD patients, informants, and clinicians (Teri & Wagner, 1991). To do this they obtained three separate total scores on the HAM-D (Hamilton, 1960); one using self-report information only, one using caregiver information only, and one in which the geriatricians used both the self-report and caregiver report as well as their own behavioral observations to come up with a score. The geriatrician used this score and DSM-III criteria to diagnose depression. All 75 patients in the study had DSM III-R diagnosis for primary degenerative dementia of the Alzheimer's type (AD). Participants in this study were predominantly female (68%). Caregivers consisted of spouses (51%), daughters (27%), sons (13%), and others (9%). The authors found that Alzheimer's patients diagnosed as depressed according to the clinical diagnosis reported less insomnia, change in interests, psychic anxiety, and somatic energy change than did the caregiver or the clinician, and that they reported less depressed mood, suicidal feelings, and somatic anxiety than the caregiver. Alzheimer's patients without depression exhibited similar findings; they reported less depressed mood and less change in interests than the caregiver or the clinician, and they reported less agitation, psychic anxiety, and somatic energy change than the clinician. It also found that caregivers reported less agitation and somatic energy change than did the physician. In addition, the study found that severity of dementia did not affect rating. Few other studies addressed the extent to which degree of cognitive impairment of the elderly

subject and background factors on the informant influence the association between multiple sources.

Conclusion

Depression among the elderly is a major public health concern. Accurate diagnosis of depression is needed in clinical practice and in epidemiological studies of cognitive impairment. Research literature reveals that, in general, subjects are less likely to report depression than other sources. Several factors contribute to this. Some studies have found that cognitive impairment affects patient self-reports of depression, with patients with cognitive impairment reporting less depression than informants or physicians. Other studies have found that social stigma inhibits patients from fully disclosing depression. Social stigma may affect informant reports of depression as well. Presence of depression itself tends to decrease reports of depression. Since depression is a side effect of some medications and medical conditions, patients and informants may view depression as "normal" and not noteworthy. The literature on the accuracy of informant reports is mixed. Some evidence suggests that type of informant and informant age affects depression reports. However, very few studies have explored how informant factors affect depression reports. Although physician evaluations are free of much of the reporting bias inherent in self-reports or informant reports, they are often not feasible in epidemiological studies.

The preceding findings lead to the following research questions.

1. What is the strength of association between subject self-report, informant

report, and physician reports of major depression?

2. Is the association between subject self-report and physician report of major depression, and the association between subject self-report and informant report of major depression, affected by subject characteristics including: subject age and gender, degree of cognitive impairment, medical comorbidities, use of medications with depressogenic side effects, or prior history of major depression?

3. Is the association between informant report and subject self-report of major depression, and the association between informant report and physician report of major depression, affected by informant characteristics including: informant age, informant relation to subject, how long the informant has known the subject, or by frequency of contact with the subject?

CHAPTER III

METHODS

This chapter describes an extant dataset made available for this thesis project. Subject selection, procedures, measurement and analyses relating to stated research questions will also be described, after first providing a brief overview of the original study.

Overview of the Cache County Study on Memory Health and Aging

The Cache County Study on Memory Health and Aging (CCSMHA) is a large, population-based epidemiological study of dementia. Funded continuously since 1994 by the National Institute on Aging (R01-AG-11380), it was designed to study prevalence and incidence of Alzheimer's disease (AD) and other dementias, and the influence of genetic and environmental factors, and their interactions, on disease risk. This was accomplished by a large-scale data collection effort at each of four triennial "waves" of ascertainment of dementia and depression (an important potential confounder when diagnosing dementia). Data sources included self-report, informant-report, and physician assessment. Because all of the depression measures required for this thesis project were not collected until Waves 3 and 4, data derive from these two study waves, with the exception being depression data from Waves 1 and 2 used only to establish prior depression history.

Subjects

The CCSMHA is a population-based study that sought to enroll 100% of eligible residents of Cache County aged 65 years or older as of January 1, 1995. The final sample for this thesis project included 1,481 subjects who completed a clinical assessment (hereafter referred to as the "CA visit") in either Wave 3 or 4, and 148 subjects who completed a physician assessment (hereafter referred to as the "MD visit") in either Wave 3 or 4. What follows is a description of the final derivation of this sample, beginning from the original eligible pool of individuals.

The original list of eligible individuals came from Medicare enrollee lists from the Health Care Financing Administration (HCFA) of those with permanent residence in Cache County, Utah, who were aged 65 years or older as of January 1, 1995. A small number were recruited from other sources such as local publicity efforts. Eligible participants totaled 5,677 when fieldwork began in April 1995. Total number of participants enrolled in the study was 5,092. The high participation rate of 90% greatly reduced non-response bias (Norton, Breitner, Welsh, & Wyse, 1994), which would tend to underestimate prevalence and incidence rates of both dementia and depression, owing to the higher probability of those who refuse participation to have greater cognitive impairment, to be older, and have less education, and to be depressed, all of which factors being related to dementia risk (Welsh-Bohmer et al., 2006).

Cache County was selected for this study for several reasons. It was reported to have the highest longevity rate in the U.S. (Murray, Michaud, & McKenna, 1998). Based on 1990 Census data, women's life expectancy was 88.1 years (compared to U.S. rate of

78.5 years) and men's life expectancy was 85.7 years (compared to U.S. rate of 71.5 years). Greater longevity substantially improves a study's ability to examine prevalence and incidence rates of conditions that afflict those in older age groups such as dementia. These reduced mortality rates are in part due to a religious denomination—The Church of Jesus Christ of Latter-day Saints—which proscribes alcohol and tobacco use. Of the local population of older adults, 91% are members of this religion (Norton et al., 2006a). The population of Cache County is associated with reduced rates of alcohol and tobacco use, resulting in reduced rates of several common cancers, hypertensive and atherosclerotic cardiovascular disease, and lower rates of mortality before age 85. These characteristics also help simplify the differential diagnosis of dementia. This population is also associated with larger families, which provides more opportunities for informant interviews. Higher rates of education found in Cache County also simplified the diagnosis of dementia; since subjects typically started higher on cognitive screening instruments, declines over time could be more readily detected. In addition, Cache County has low rates of in and out migration, which leads to greater participant consistency. This consistency is of great benefit in longitudinal studies.

Of the population of persons 65 years or older identified in Cache County, 542 refused interviewing, 26 were deceased, and 17 could not be located, leaving 5,092 participants. Of these, 371 were identified in Wave 1 as having dementia, leaving 4,721 persons who were eligible for the Wave 2. Of these 4,721 persons, 594 were deceased, 159 moved away, 546 refused interviewing, and 15 could not be located, leaving 3,407 persons who participated in Wave 2. Wave 2 identified 204 of these persons as having

dementia, leaving 3,203 eligible for Wave 3.

In Wave 3, 2,324 persons participated in the screening assessment, while 97 persons were deceased, 75 had moved away, 354 refused, 25 persons could not be located. The researchers selected participants for the CA visit if at the screening assessment the participants were 85 years of age or older, if they had screened positive (score of 90 or lower) on the Modified Mini-Mental State Examination (3MS; Teng & Chui, 1987), or if they were selected to be part of a designated control panel (details provided below). Of the 2,324 completing screening in Wave 3, 1,593 were selected for the CA (68.5%), and of these 1,224 (76.8%) completed the CA, while 74 were deceased, 24 had moved or were not located, and 271 refused. Participants that were given a provisional diagnosis of dementia or "mild/ambiguous" impairment (subsyndromal AD) at the case staffing review of the CA visit were selected for the physician evaluation. Of the 1,229 completing the CA visit, 423 participants were selected for the MD visit (34.6%), and of these, 357 (84.4%) completed the MD visit27 were deceased, 4 had moved or could not be located, and 35 refused.

To ensure independence of observations, only one set of data was used for each subject. If a subject completed the CA and/or MD visit at both Waves 3 and 4, only the data from Wave 3 were used (this protocol is described in more detail in Appendix B, along with analyses to determine similarity across several demographic measures between subjects whose data came from Wave 3 versus Wave 4). As a result of this protocol, this study utilized data from the 1,229 persons who participated in the Wave 3 CA visit and an additional 252 who did not participate in Wave 3 CA visit but did

participate in Wave 4 CA visit (total with data from the CA is *n* = 1,481). In analyses of MD visit data, this study utilized data from 124 persons who completed Wave 3 MD visit measures and an additional 24 persons who completed the measures at the Wave 4 MD visit.

Procedures

Of primary interest are procedures involved in the collection of depression data analyzed in the present work. However, the sample for this thesis project was comprised of the subset of participants who completed the more in-depth clinical data gathering portion of the CCSMHA. Therefore, what follows next is a detailed description of procedures employed to determine this final sample, including procedures for the CA and MD visits where depression data were gathered.

The CCSMHA study included four ascertainment "waves," spaced approximately 3-4 years apart. The first wave was designed to identify prevalent cases of dementia and later waves to identify incident cases. At each wave, participants completed a three-stage dementia screening protocol, which consisted of a cognitive screening, a clinical assessment (CA visit), and a physician evaluation. Ascertainment protocol was modified in Waves 3 and 4. Given that these are the waves from which data was utilized for this thesis, protocol for these waves are described here.

In the first stage, researchers conducted screening interviews to collect both cognitive data and information on interval putative risk factors. Cognitive screening consisted of the 3MS (Teng & Chui, 1987). The 3MS is a 100-point adaptation of the Mini-Mental State examination (MMSE; Folstein et al., 1975) that increases the

instrument's floor and ceiling. Researchers further adapted the 3MS for epidemiological studies (Tschanz et al., 2002), including alternate versions of the test that included two new word list recall tasks in addition to the original tasks. Informants (typically spouses or other family members) were used to collect risk-factor interview data if the subject (a) could not complete the 3MS, (b) scored below 15 out of 20 on a set of orientation questions asked at the beginning of the interview, (c) scored below 60 on the 3MS, or (d) was for any other reason deemed by the clinical judgment of the interviewer as unreliable. In all other cases, subjects gave their own risk factor interview data, including information about depression using a modified version (Steffens et al., 2000) of the Diagnostic Interview Schedule's Depression Scale (DIS; Robins, Helzer, Croughan, & Ratcliff, 1981). Informants were given the Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE; Jorm, 1994). This instrument assessed the extent to which the subject's cognitive abilities had declined over the preceding 4-year and 10-year intervals. Higher scores on this measure indicate greater impairment. Informants were also asked the same set of risk factor questions, including a third-person version of the depression interview.

Participants with a positive cognitive screening, defined as a score less than or equal to 90 points out of 100 on the 3MS (adjusted for education and sensory impairments) or an IQCODE composite score greater than or equal to 3.27, were selected for CA visit. Also selected for CA were members of a designated control panel initially selected in Wave 1 (Breitner et al., 1999), which was replenished in Wave 3 with additional random sampling to replace members lost to attrition. This designated control

panel was randomly stratified for age, gender, and APOE genotype, weighted to yield a 2:1 ratio of controls to persons with a positive cognitive screening, except for the youngest two strata (65-69 and 70-74 years) with zero or one e4 allele at APOE for whom a 4:1 ratio was used. In addition, all participants 85 years of age and older were selected for the CA visit. Thus, a substantial portion of those completing the CA visit were not selected due to positive screening results. Consequently, the final sample of CA visit participants is a more heterogeneous mix of subjects who were cognitively normal, had mild cognitive impairment, or had dementia.

The CA visit included a brief neurological exam, a clinical history from an informant (typically spouse or adult child of the subject), an informant-based Neuropsychiatric Inventory, the Patient Health Questionnaire-9 (PHQ-CA), and a battery of neuropsychological testing, administered by a trained psychometrician. A board certified geriatric psychiatrist and neuropsychologist reviewed the testing from the CA visit with the examiners in "case staffing" reviews. After review they assigned participants to working diagnoses of dementia (according to DSM-III-R criteria), vascular dementia (according to NINDS-AIREN criteria; Roman et al., 1993), AD, probable AD, possible AD (according to NINCDS-ADRDA criteria; McKhann et al., 1984) or other classifications, such as dementia of unknown etiology, demented-not AD, mild/ambiguous (not meeting criteria for dementia, with suspected prodromal AD), or other (cognitive symptoms dissimilar from prodromal AD, such as a stroke or schizophrenia), and noncase.

Only those subjects with a provisional diagnosis of dementia or prodromal

Alzheimer's disease were selected for the physician evaluation. Physicians rendered a new working cognitive diagnosis (blinded to the initial diagnosis rendered at the CA case staffing meeting). This diagnosis matched the CA case staffing diagnosis for 167 of the participants (65%). Discrepancies were generally minor for the other participants (e.g., "possible AD" versus "probable AD"). A final diagnosis was obtained after all these procedures by consensus of an expert panel of specialists. One or more board certified geriatric psychiatrists, neurologists, neuropsychologists, and neuroscientists reviewed all information and assigned participants a final diagnosis from a list of 30 differential diagnostic categories.

Use of human subjects and all procedures employed were approved by the Institutional Review Boards of Duke University Medical Center, the Johns Hopkins Bloomberg School of Public Health, and Utah State University. Written informed consent was obtained prior to every interview.

Measurement Scales

Of all the measures collected on study participants at the screening visit, the CA visit and the MD visit, only those pertaining to assessment of depression are included in the present work. Each is described in more detail below, including psychometric properties.

The *Diagnostic Interview Schedule –Depression Scale (DIS*; Robins et al., 1981) was completed at the screening visit of each wave, and was used in the present work to derive a "prior major depression history" subject characteristic variable (coded as positive/negative report of major depression, up to and including Wave 2). No other

depression measure was collected at the screening visit, so this visit does not contribute depression data from multiple sources, the focus of this project.

The DIS assesses a variety of psychological disorders. Both clinicians and lay interviewers can administer this measure. The DIS yields lifetime and recent diagnoses, as well as onset of recent diagnoses (occurred in last 2 weeks, last month, last 6 months, or last year). To ascertain whether lay interviewers could reliability administer the DIS in the place of clinicians, Robins et al. assessed agreement between lay interviewer and psychiatrists on lifetime diagnosis (Robins et al., 1981). Overall, Kappa statistics for showed good agreement ($\kappa = .63$). Overall sensitivity and specificity were also good (80% and 84%, respectively), as was sensitivity for current patients (sensitivity = 79% and specificity = 81%) and former patients (sensitivity = 82% and specificity = 67%).

The Cache County study modified the DIS by including three "gateway" questions asking whether the subject had experienced two or more consecutive weeks of sadness, anhedonia (inability to experience pleasure from life events that are normally pleasurable), or irritability. If respondents endorsed at least one of these three symptoms then interviewers asked DIS questions dealing with specific symptoms, including appetite or weight change, sleep or concentration difficulties, guilt, restlessness, diminished energy level, or suicidal ideation. Interviewers also asked for year, month, and symptoms of any depressive episodes that had happened during the preceding wave interval. Diagnosis of major depression was assigned following Blazer, Hughes, and George (1987), when subject endorsed five or more DIS symptoms (one of which being sadness or loss of interest).

Patient Health Questionnaire (PHQ-9) is the 9-item depression module of the PHQ, a multi-diagnostic instrument which itself is a brief form of the Primary Care Evaluation of Mental Disorders (PRIME-MD; Spitzer, Kroenke, & Williams, 1999) scale. In the CCSMHA, the PHQ-9 was self-administered. Major depressive disorder is characterized by the instrument as five or more of the nine depressive symptoms for at least "more than half the days" in the past 2 weeks, with one of the symptoms being depressed mood or anhedonia. Each of the nine DSM-IV criteria is scored on a "0" (not at all) to "3" (nearly every day) severity scale, resulting in a total score that can range from 0 to 27 points. Scores of 5, 10, 15, and 20 on the PHQ-9 indicate mild, moderate, moderately severe, and severe depression, respectively. Subjects exhibiting any symptoms answer a question about the functional impact of the disorder.

The PHQ-9 has demonstrated adequate construct validity (Kroenke et al., 2001). PHQ-9 scores were compared with clinician diagnoses of depression, where the clinicians utilized the Structured Clinical Interview for DSM-III-R (Spitzer et al., 1992) and diagnostic questions from the PRIME-MD (Spitzer et al., 1999) in reaching diagnoses. Kroenke and colleagues found that 93% of participants diagnosed as non-depressed by the clinician had scores lower than 10 on the PHQ-9, and 88% of participants diagnosed as having major depression by the clinician had scores of 10 or greater on the PHQ-9. The PHQ-9 was collected at the CA and the cutoff ($\geq$ 10) was used in the present study to indicate major depression. For my analyses, I used only participants that had responded to most of the items on this measure (at least five out of the nine items). If these subjects had any missing responses, I added to the total score the mean of the non-missing

responses for each item that was missing. This method is described in further detail in Appendix B.

Neuropsychiatric Inventory (NPI; Cummings et al., 1994) uses semi-structured interviews to measure ten behavioral domains, with depression/dysphoria being the only domain examined for this thesis. Informants are given a gateway question, in which they are asked if the subject has seemed sad or depressed in the previous four weeks. If the answer is affirmative, 15 subquestions are asked. After asking the subquestions, the interviewer asks questions about the frequency of symptoms, coded as: 1 = occasionally, less than once per week; 2 = often, about once per week; 3 = frequently, several times per week but less than every day; 4 = very frequently, once or more per day or continuously. Severity is coded as: 1 = mild, 2 = moderate, 3 = severe. Frequency and severity scores are multiplied together to yield the NPI raw depression score that can range from 0-12 (Steinberg et al., 2004). The NPI can be administered by a variety of professionals. The CCSMHA collected the NPI at the CA via research nurse and at the physician evaluation by the geropsychiatrist, using identical scoring protocols.

The NPI was found to have good content validity, construct validity, and reliability (Cummings et al., 1994). A panel of 10 geriatric psychiatry experts rated NPI items on how well they represented the essential nature of the behavior. Mean rating was 1.2 (1 = good, 4 = poor) for the depression/dysphoria screening question and 1.3 for the depression/dysphoria subsections. Construct validity was also good; Spearman correlations comparing frequency, severity, and frequency x severity depression/ dysphoria scores with the “affective disturbances” subscale score of the Behavior

Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD; Reisberg et al., 1987) were 0.54, 0.47, and 0.33, respectively. Internal consistency was adequate (Cronbach's alpha = 0.88). Only 22% of the items were correlated, demonstrating adequate item independence. Inter-rater reliability was 97.9% for both frequency and severity of depression/dysphoria. Test-retest reliability was also good; coefficients were 0.79 and 0.84 for frequency and severity, respectively. Following Schneider and colleagues (2001), I used a cutoff of ≥ 4 to indicate major depression. For my analyses, I used only participants that had a non-missing response to the gateway question. No participants at the MD visit, and less than 1% of participants at the CA visit were missing responses to this question.

Geriatric Depression Scale (GDS; Yesavage et al., 1982) is specially designed for the elderly. For this measure, subjects respond yes or no to each of its 30 items related to current depressive symptoms. In 20 of the questions a "yes" response indicates depression, while in the other 10 questions a "no" response indicates depression. One point is given for each item indicating depression, yielding a possible range of 0-30 points. Because researchers began collecting data on this measure part way through the Wave 3 MD visit, not all persons that participated in this visit were given this measure.

Yesavage and colleagues (1982) confirmed the validity and reliability of the GDS. Construct validity was demonstrated in that this measure correlated well with other depression measures (HAM-D): $r = .83$, and Zung Self-Rating Depression Scale (SDS): $r = .84$], and was further demonstrated in that mean GDS scores were found to be increasingly greater in participants characterized as normal, mildly depressed, and

severely depressed according to research diagnostic criteria (RDC; Spitzer, Endicott, & Robins, 1978). In addition, the authors found the GDS to be reliable. Median correlation of items on the GDS with its total score (r =.56) was comparable to that of other depression measures (HAM-D: r =.44, and SDS: r =.56]. Mean correlation among all GDS items (r =.36) was comparable to mean correlation among all HRS-D items (r =.25) and among all SDS items (r =.34). Cronbach's alpha for the GDS was high (r =.94), as was split-half reliability (r =.94), and test-retest reliability (r =.85).

The present study used a GDS cutoff score of ≥10 to indicate major depression. A study by Lyness and Noel (1997) found that this cutoff achieved a sensitivity of 100% and a specificity of 84% when compared with the Structured Clinical Interview for the DSM III-R (Spitzer et al., 1992). For my analyses, one participant was missing responses on 27 of the 30 items, and so was removed. The remaining participants were missing no more than 3 of the 30 items.

Physician's Clinical Rating of Depression was also completed during the in-home physician evaluation. Because researchers began collecting data on this measure part way through the Wave 3 physician evaluation, not all persons that participated in this visit were given this measure. This assessment was conducted by geriatric psychiatrists and internal medicine physicians with a specialty in geriatric psychiatry. Assessment protocol (see Appendix A) given to physicians stated that they could review the most current NPI and the GDS from the MD visit, and also that they could gather information from subjects during the visit. To aid diagnosis, the protocol also included a list of major depressive symptoms and guidelines on diagnosing minor depressive disorder, bipolar

disorder, and mood disorder not otherwise specified (NOS). The protocol instructed physicians to classify participants into one of five categories: no current depression, current major depressive episode, current minor depressive episode, mood disorder NOS, and bipolar disorder. The present study categorized participants as to whether the physician rated them to have major depression. Acknowledging that this physician evaluation did not include a full psychiatric evaluation for depression, the diagnoses rendered represent the physicians' best "clinical impression" of the subject's current depressive state, for the purpose of assigning subjects to "working research diagnoses."

Summary of depression measures. Table 1 lists the depression measures that were compared. At the CA, the strength of association was evaluated between the PHQ-9 and the NPI. This comparison had a sample size of 1,481 subjects. At the MD visit, the following associations were evaluated: the GDS versus the NPI, the GDS versus the Physician's Clinical Rating of depression, and the NPI versus the Physician's Clinical Rating of depression. There were 136 cases used for these comparisons. To facilitate the reporting of findings, I will hereafter refer to the PHQ-9 and the NPI from the CA visit as the "CA-Self" and the "CA-Informant," respectively, and to the GDS, the NPI from the MD visit, and the Physician's Clinical Rating of depression as the "MD-Self," the "MD-Informant," and the "MD-Doc," respectively. Table 2 reports the distribution of each depression measure as a continuous variable.

Subject characteristics. Subject gender was noted at the initial interview and age was recorded at each interview. To define subject cognitive status, the final expert-consensed diagnosis from the CA was used, coded into the trichotomy of: noncase, mild/

Table 1

Depression Measures

		CA (*n* = 1,481)		MD (*n* = 148)
Report type	Instrument	Major Dep. Criteria	Instrument	Major Dep. Criteria
Self-report	CA-Self	≥ 5	MD-self	≥ 10
Informant report	CA-Informant	≥ 4	MD-informant	≥ 4
Clinician report	N/A	N/A	MD-doc [a]	0-1

[a] MD-Doc = Physician's Clinical Rating

Table 2

Distribution of Depression Measures

Report type	Scale	Min	Max	Mean	*SD*
CA-Self[a]	0-27	0	23	3.3	3.9
CA-Informant[b]	0-12	0	12	0.4	1.4
MD-Self [c]	0-30	0	19	6.7	4
MD-Informant	0-12	0	12	1.3	2.6

[a] CA-Self =Patient Health Questionaire-9,
[b] CA/MD-Informant= Neuropsychiatric Inventory from
[c] CA or MD visit, MD-Self = Geriatric Depression Scale,

other cognitive impairment, and dementia, for analyses of CA visit data, but coded into only the latter two categories for analyses of MD visit data (since noncases did not complete this visit). Prior depression history was dichotomized into "major depression" versus "no major depression" spanning the subjects lifetime from birth through the Wave 2 screening visit.

Data on medical conditions and use of medications with depressogenic side effects were also available. These medications included interferon, and medications from the following classifications: beta blockers (e.g., atenalol, propranolol, metoprolol are some generic names; *Physician's Desk Reference*, 2010) and steroids (e.g., prednisone; (Brown, Vera, Frol, Woolston, & Johnson, 2007). Medication information was recorded at the CA visit, and was updated by the physician at the MD visit. Information on medical conditions was collected at each of the screening visits. Because many subjects had at least one medical condition, subjects were dichotomized into whether they had two or more of the following conditions at any of the four waves: heart attack, stroke, hypertension, diabetes, and hypercholesterolemia, or a coronary artery bypass graft.

Informant characteristics. Informant characteristics included relation to subject, frequency of contact with the subject, age, gender, and how long informants had known the subject. Relation was defined as spouse versus non-spouse. Frequency of contact was defined as those who lived with the subject versus those who did not live with the subject. Age was categorized as less than 65 years old versus 65 years old or older. How long the informant had known the subject was defined as less than 55 years old versus 55 years old or older. To assess whether the informant relationship with the subject and the number of years the informant had known the subject were too highly correlated to justify examination of each as distinct moderators, I computed Pearson correlations between these factors. This analysis, summarized in detail in Appendix B, found these factors to be distinct constructs, permitting separate examination of each as a potential moderator of associations between depression reports.

Data Analysis

Because elapsed time between visits in the CCSMHA multi-stage dementia ascertainment protocol varied from 3 to 24 months, analyses conducted for this thesis project were restricted to those comparing depression measures within visits. This avoids analyses where data source (self, informant, physician) is confounded with elapsed time. When comparing depression reports between sources and across time, it would not be possible to disentangle extent of disagreement attributable to each of these two factors. Additionally, covarying elapsed time would not be sufficient to "correct for" depression remission or new-onset depression occurring over the interval.

Research Question 1

To ascertain the prevalence of major depression as reported by subjects, informants, and physicians, I computed the prevalence of major depression on each measure, along with the overall prevalence of major depression at each visit, collapsing over the multiple depression assessments and counting as depressed if any measure was coded as positive for depression.

To assess basic agreement between these sources, I reported crosstabulations within each of the source comparisons examined in this study. Also, I calculated the Kappa statistic, a measure of inter-rater agreement of categorical data, which differs from traditional inter-rater agreement statistics in that it assesses the proportion of agreement beyond agreement which can be attributed to chance. It is computed by dividing the number of cases for which raters agree by the total number of cases, subtracting from this

the proportion of cases for which agreement between raters could be attributed to chance, and then dividing this number by proportion of cases for which agreement cannot be attributed to chance. Because raters are more likely to agree that a condition is not present if the prevalence of the condition is low, the proportion of cases for which agreement between raters could be attributed to chance is computed by taking into account the average prevalence of the condition across raters. A Kappa score of 1 indicates perfect interrater agreement, a Kappa score of 0 indicates no agreement other than that expected by chance, and Kappa scores less than 0 indicate less agreement than that expected by chance. To test the statistical significance of Kappa, a null hypothesis of 0 is used, and p values are calculated using the normal distribution (Sim & Wright, 2005). Table 3 lists the strength of agreement for different ranges of Kappa values as suggested by Landis and Koch (1977).

To further assess the associations between self-report, informant report, and the physician report I used Logistic Regression (LR), with the rationale that this approach would also facilitate tests of moderation through inclusion of interaction terms, as needed

Table 3

Strength of Agreement of Values of Kappa

Kappa statistic	Strength of agreement
<.00	Poor
0-0.20	Slight
.21-.40	Fair
.41-.60	Moderate
.61-.80	Substantial
.81-1.00	Almost perfect

to address Research Questions 2 and 3 (see below). In models including the MD-Doc, I regressed MD-Doc on MD-Informant and MD-Self, since this measure is hypothesized to be the "gold standard."

In logistic regression models comparing subject and informant reports, I regressed subject rating on informant rating in both instances (i.e., MD-Self was regressed on MD-Informant, and CA-Self was regressed on CA-Informant). Comparisons between informant and subject measures (whether using Kappa or logistic regression) did not involve a gold standard, and thus did not ascertain which source is more accurate. It does, however, indicate the extent to which these sources agree.

Significance in logistic regression models was determined by the Wald and -2 log likelihood change (-2LL change) statistics. The -2LL change statistic represents the improvement in fit that results from adding a term to the model, which in this case would be the depression measure entered as the predictor variable. This statistic is computed by subtracting the -2LL statistic from the model with the term in it (in this case, the model with the depression variable entered) from the -2LL statistic from the model without the term in it (in this case, the intercept only model). Since this statistic is distributed as a chi-square statistic, one can determine the significance of this value using a chi-square significance table. Typically (though not always) the Wald and -2LL test results are consistent, but I took the conservative approach in considering the test of association between the two measures to be significant only if both test statistics were significant at the $p < .05$ level.

In addition, to assess the cut points on the MD-Self and MD-Informant that most

closely predict major versus no major depression on the MD-Doc, receiver operating characteristic (ROC) analyses were planned but not conducted because of sample size issues.

Research Question 2

To assess whether the associations between self-reports, informant reports, and physician's reports are affected by subject characteristics; original regression models were expanded to include subject moderators and their interaction with depression measures. A significant interaction term, which was indicated when the Wald statistic and the -2LL change statistic (difference between -2LL between model with and model without interaction) were significant at the $p < .05$ level, signified that the association is moderated by the subject characteristic tested in the interaction term. Subject moderators were tested in all four source comparisons: CA-SELF versus CA-Informant, MD-Self versus MD-Informant, MD-Doc versus MD-Self, and MD-Doc versus MD-Informant.

Each subject characteristic was analyzed separately for potential moderating effects. In the MD-Doc versus MD-Self model that tested the dementia moderator, only the MCI/OCI and demented categories were used because cognitively normal persons did not go to the MD visit. When a subject characteristic had a significant interaction (i.e., was found to be a moderator), I then conducted models that included only the source comparison, stratified by each level of the subject characteristic. For example, if the interaction term that included subject gender was significant, I ran the model that included the source comparison among only males, and then the same model among only females. These analyses revealed the manner in which the source comparison was

affected by the subject characteristic. For instance, the stratified models could reveal that the source comparison was significantly associated within only one level of the moderator, or they could reveal that the source comparison was more strongly associated in one level of the moderator than in another, possibly even in opposite directions. Each of the subject characteristics was tested for potential moderation on the condition that adequate sample size conditions were met. Two such conditions had to occur. First, that of the 1,481 subjects that participated at the CA visit at either Wave 3 or Wave 4, and of the 148 subjects that participated at the MD visit at either Wave 3 or Wave 4, each subject moderator had to have no more than 20% missing data. Second, each three-way cross-tabulation between the subject moderator and its respective source comparison had to contain enough cases in its cells for the model to converge.

Research Question 3

For Research Question 3, to assess whether the association between sources was affected by informant characteristics, the same approach was used as in Research Question 2; original regression models were expanded to include informant variables and their interaction with depression measures. Significant interaction terms indicated that the association was moderated by the informant characteristic tested in the interaction term, and for informant characteristics with significant interactions, I conducted separate models stratified by each level of the informant moderator. Informant moderators were tested in each of the four source comparisons: CA-SELF versus CA-Informant, MD-Self versus MD-Informant, MD-Doc versus MD-Self, and MD-Doc versus MD-Informant. As with Research Question 2, each of the informant characteristics was tested on the

condition that each informant characteristic had no more than 20% missing data, and that each three-way cross-tabulation between the informant characteristic and its respective source comparison had enough cases in its cells for the model to converge.

CHAPTER IV

RESULTS

This chapter reports results of statistical analyses described in the previous chapter, to address each of the three research questions in this thesis. Given that there were two depression measures collected at the CA and three depression measures collected at the MD visit, there are four within-visit comparisons targeted. These include: CA-SELF versus CA-Informant, MD-Self versus MD-Informant, MD-Self versus MD-Doc, and MD-Informant versus MD-Doc, results of which are reported in this chapter, in this order, within each research question. Additionally, when reporting results for Research Questions 2 and 3, not every subject and informant characteristic was able to be examined for moderator effects, due to data limitations. Nevertheless, within each of these two sections, I have provided some information—either results of statistical analysis or explanation as to data limitation(s) that precluded their examination. This information is provided for each of the subject and informant characteristics targeted in the prior chapters of this thesis, in the same order, within each research question.

Research Question 1

Research question 1 sought to assess the strength of association between subject self-report, informant report, and physician reports of depression. Table 4 reports the prevalence of major depression on each measure for each visit, which ranged from 4.4% to 23.5%, depending on the measure. This table also indicates that subjects were more likely to report major depression than physicians, and that subjects were more likely to

Table 4

Prevalence of Major Depression Per Measure and Per Visit

CA-Self[a]	CA-Informant[b]	CA visit prevalence[e] (*n* = 1,481)	MD-Self[c]	MD-Informant	MD-Doc[d]	MD visit prevalence[f] (*n* = 148)
8.4%	4.4%	11.4%	23.5%	13.4%	7.4%	31.8%

[a] PHQ = Patient Health Questionaire-9.

[b] CA/MD-Informant = Neuropsychiatric Inventory from CA or MD visit.

[c] MD-Self = Geriatric Depression Scale.

[d] MD-Doc = Physician's Clinical Rating.

[e] Proportion of participants who met criteria for major depression on one or more CA depression measures.

[f] Proportion of participants who met criteria for major depression on one or more MD visit depression measures.

report major depression than informants. It also indicates that informants are more likely to report major depression than physicians. Generally, prevalence of depression was higher at the MD visit than at the CA visit. In addition to reporting the prevalence of major depression on the MD-DOC, in Table 5 I also reported the frequency of each diagnostic category from that measure. This table indicates that minor depression and mood disorder were about as common as major depression, and that bipolar disorder was not diagnosed at all. Tables 6 through 9 report crosstabulations within each of the source comparisons examined in this study. In general, these tables indicate higher agreement between the informant and the physician than between the subject and either the informant or the physician.

Tables 10 and 11 report results from Kappa statistics that tested the agreement between source, and from logistic regression models that tested the overall association between sources. Agreement between subject and informant reports of depression was poor. Although the Wald statistic and the -2LL change are significant in the model

Table 5

Number of Persons Diagnosed into Each Category of MD-DOC

Diagnostic category	Frequency	%
No current depression	111	75
Current major depressive episode	11	7.4
Current minor depressive episode	11	7.4
Mood disorder	15	10.1
Bipolar disorder	0	0
Total	148	

Table 6

CA-Self by CA-Informant

	CA-Informant					
	no major depression		major depression			
CA-Self	*n*	%	*n*	%	total	%
No major depression	1,197		43		1,240	91.8
Major depression	100		11		111	8.2
Total	1,297	96	54	4	1,351	100

Table 7

MD-Informant by MD-Self

	MD-Informant					
	no major depression		major depression			
MD-Self	*n*	%	*n*	%	total	%
No major depression	68		9		77	75.5
Major depression	20		5		25	24.5
Total	88	86.3	14	13.7	102	100

Table 8

MD-Doc by MD-Self

	MD-Doc					
	no major depression		major depression			
MD-Self	*n*	%	*n*	%	total	%
No major depression	99		5		104	76.5
Major depression	28		4		32	23.5
Total	127	93.4	9	6.6	136	100

Table 9

MD-Doc by MD-Informant

	MD-Doc					
	no major depression		major depression			
MD-Informant	*n*	%	*n*	%	total	%
No major depression	89		4		93	86.1
Major depression	10		5		15	13.9
Total	99	91.7	9	8.3	108	100

Table 10

Kappa for Source Comparisons

Source comparison	Kappa
MD-Doc[a] / MD-Self[b]	0.1
MD-Doc / MD-Informant[c]	0.35***
CA-Self[d]/ CA-Informant	0.08***
MD-Informant / MD-Self	0.01*

[a] MD-Doc =Physician's Clinical Rating.
[b] MD-Self = Geriatric Depression Scale.
[c] CA/MD-Informant=Neuropsychiatric Inventory.
[d] PHQ-=Patient Health Questionaire-9.
*$p < .05$
*** $p < .001$

Table 11

Regression Models for Overall Source Comparisons

Source	*n* size	*OR*	95% CI of *OR*		Wald	-2LL change
CA-Self [d] / CA-Informant [e]	1,351	3.1	1.5	6.1	10.1**	8.2**
MD-Informant / MD-Self [f]	102	1.9	0.6	6.3	1.1	1
MD-Doc [a] / MD-Self [b] [g]	136	2.8	0.7	11.2	2.2	2.1
MD-Doc [a] / MD-Informant [c] [h]	108	11.1	2.6	48.3	10.3**	9.9**

[a] MD-Doc =Physician's Clinical Rating.
[b] MD-Self = Geriatric Depression Scale.
[c] CA/MD-Informant = Neuropsychiatric Inventory.
[d] PHQ = Patient Health Questionaire-9.
[e] CA-SELF regressed on CA-Informant.
[f] MD-Informant regressed on MD-Self.
[g] MD-Doc regressed on MD-Self.
[h] MD-Doc regressed on MD-Informant.
*$p < .05$.
** $p < .01$.

assessing the association between the CA-Self and the CA-Informant ($p < .01$), the Kappa statistic was only .08 ($p = .001$), indicating poor agreement. Table 11 also contains results from the model comparing the MD-Informant and the MD-Self. For this model, the Wald statistic, the -2LL change, and the Kappa statistic ($\kappa = .1$, $p = .30$) were not significant.

Subject reports and physician reports of depression were found to be virtually unrelated. In the model comparing the (MD-Doc) and the MD-Self, neither the Wald statistic nor the -2LL change are significant, indicating that the MD-Self cannot predict outcomes on the MD-Doc. The Kappa statistic for these measures ($\kappa = .1$, $p = .13$) was also not significant.

In contrast, informant reports and physician reports were related, and the association between these sources was moderate. In the model comparing the MD-Doc and NPI informant reports from the MD visit, both Wald statistic and -2LL change are

significant at the $p < .01$ level, and Kappa indicates fair agreement ($\kappa = .35$, $p < .001$). Because only nine persons were diagnosed with major depression on the MD-Doc, I was unable to conduct ROC analyses, which were designed to find the optimal cutoffs on the MD-Self and MD-Informant for predicting cases and noncases on the MD-Doc.

Research Question 2

Research question 2 seeks to ascertain whether the association between subject self-report and physician report of major depression, and the association between subject self-report and informant report of major depression, are moderated by subject characteristics. Table 12 summarizes demographic characteristics of subjects. This table indicates that on none of these characteristics are subjects missing more than 20% of the data. However, in the MD-Doc by MD-Self model that included the subject age moderator, and in the MD-Doc by MD-Informant models that included the subject age and prior depression history moderators, crosstabulations indicated sparse data in some cells that precluded testing this moderator (see Tables B17, B23, and B25, respectively, in Appendix B).

CA-Self Versus CA-Informant

Table 13 reports interactions from the CA-Self by CA-Informant source comparison. Nearly all of the Wald and -2LL statistics testing for significant moderation by subject characteristics were not significant, indicating no moderating effects of the examined variables. The exception was the cognitive status moderator. The Wald and -2LL change statistics for the interaction are not significant. However, the Wald statistic

Table 12

Demographic Summary of Subjects

	CA visit		MD visit[a]	
Variable	*n*	%	*n*	%
Subject gender				
Males	636	42.9	61	41.2
Females	844	57	87	58.8
Missing	1	0.1	0	0
Subject age				
< 85 years old	961	64.9	85	57.4
85+ years old	517	34.9	63	42.6
Missing	3	0.2	0	0
Cognitive impairment				
Normal	624	42.1	10	6.8
MCI/OCI	628	42.4	95	64.6
Dementia	228	15.4	1	.7
Missing	1	.1		
Prior depression history				
No prior depression	1,198	80.9	117	79.1
Prior depression	226	15.3	26	17.6
Missing	57	3.8	5	3.4
Medical conditions				
Had < 2 medical conditions	569	38.4	52	35.1
Had 2+ medical conditions	912	61.6	96	64.9
Missing	0	0	0	0
Medication use				
Not taken meds	1,134	76.6	113	76.4
Taken meds	346	23.4	34	23
Missing	1	0.1	1	.7

[a] Based on the total number of persons that took either the MD-Doc or MD-Self at the MD visit.

for the normal versus MCI/OCI comparison is significant at the $p < .05$ level. To further study this interaction, I stratified the CA-Self versus CA-Informant source comparison by cognitive status. Table 14 reports results for these models. As can be seen, the Wald statistic and -2LL are significant for only cognitively normal subjects, that is, only the cognitively normal subjects had significant association between these two measures. In addition, in Table 15 I report Kappa statistics for the CA-Self by CA-Informant source

Table 13

CA-Self Regressed on CA-Informant: Subject Moderators

	n size	OR	95% CI of OR		Wald	-2LL change
CA-Informant [b] x subject gender (male) [a]	1,351	1.1	0.3	4.6	0.0	0.1
CA-Informant x CA visit subject age (<85 [a] versus 85+ yrs. old)	1,349	0.2	0.0	1.6	2.4	3.3
CA-Informant x subject cognitive status (overall interaction effect)	1,351				4.0	3.6
CA-Informant x subject cognitive status (normal [a] versus MCI/OCI)	1,351	0.1	0.0	1.0	4.0*	
CA-Informant x subject cognitive status (normal [a] versus dementia)	1,351	0.3	0.0	1.9	1.7	
CA-Informant x prior dep. history (no prior maj. dep. [c] versus prior maj. dep.)	1,306	0.6	0.1	2.5	0.5	0.5
CA-Informant x med. cond. (less than two med. cond. [a] versus two or more)	1,351	2.2	0.4	12.4	0.9	1.0
CA-Informant x medications (meds taken versus not taken) [a]	1,351	0.6	0.1	3.4	0.4	0.4

[a] Reference category.

[b] NPI = Neuropsychiatric Inventory.

*$p < .05$.

Table 14

CA-Self Regressed on CA-Informant for Each Level of Cognitive Impairment

Cognitive impairment	*n* size	OR	95% CI of OR		Wald	-2LL change
Normal	592	10.1	1.9	52.6	7.6**	5.1*
MCI/OCI[a]	580	1.2	0.4	4.3	0.1	0.1
Dementia	179	2.7	0.9	7.8	3.4	3.1

[a] MCI/OCI = mild cognitive impairment/other cognitive impairment.
* $p < .05$.
** $p < .01$.

Table 15

Kappas for CA-Informant by CA-Self for Each Level of Cognitive Status

Cognitive status	Kappa	*p* value
Cognitively normal	0.13	0.001
MCI/OCI[a]	0.01	0.75
Demented	0.14	0.06

[a] MCI/OCI = mild cognitive impairment/other cognitive impairment.

comparison for each level of cognitive status. This table indicates, that although agreement between the CA-Self and CA-Informant was highest among demented persons ($\kappa = 0.14$), only agreement on these measures among cognitively normal persons ($\kappa = 0.13$) was significant.

MD-Self Versus MD-Informant, MD-Doc Versus MD-Self, MD-Doc Versus MD-Informant

Tables 16-18 report interactions used in the models testing the associations between the MD-Self and the MD-Informant, the MD-Doc and the MD-Self, and the

Table 16

MD-Self Regressed on MD-Informant: Subject Moderators

Interaction (categories)	*n* size	*OR*	95% CI of exp *b*		Wald	-2LL change
MD-Informant x subject gender (male) [a]	102	0.31	0.0	4.1	0.8	0.8
MD-Informant x MD visit subject age (< 85 [a] versus 85+ yrs. old)	102	1.3	0.1	16.7	0.0	0.0
MD-Informant x subject dementia (normal [a] versus MCI/OCI versus dementia)	94	0.5	0.0	6.0	0.4	0.4
MD-Informant x prior dep. history (no prior maj. dep. [a] versus prior maj. dep.)	98	0.1	0.0	2.8	1.7	1.8
MD-Informant x med. cond. (less than two med. cond. [a] versus two or more)	102	0.3	0.0	4.0	0.8	0.8
MD-Informant x medications (not taken [a] versus taken meds)	102	0.6	0.0	11.8	0.1	0.1

[a] Reference category

Table 17

MD-Doc Regressed on MD-Self: Subject Moderators

Interaction (categories)	*n* size	*OR*	95% CI of OR		Wald	-2LL change
MD-Self x gender (male) [a]	136	0.2	0.0	3.1	1.4	1.4
MD-Self [b] x cognitive status (MCI/OCI [a] versus demented)	126	0.5	0.0	10.6	0.2	0.2
MD-Self x prior dep. history (no prior maj. dep. [a] vs. prior maj. dep.)	131	0.3	0.0	6.3	0.7	0.7
MD-Self x medical conditions (less than two med. cond. [a] versus two or more)	136	2.2	0.1	35.0	.3	.3
MD-Self x medications (meds taken versus not taken) [a]	136	0.6	0.0	11.8	0.1	0.1

[a] Reference category

[b] MD-Self = Geriatric Depression Scale

Table 18

MD-Doc Regressed on MD-Informant: Subject Moderators

Interaction (categories)	n size	OR	95% CI of exp *b*		Wald	-2LL change
MD-Informant x subject gender (male) [a]	108	0.5	0.0	10.6	0.2	0.2
MD-Informant x subject dementia (normal [a] versus MCI/OCI versus dementia)	99	0.5	0.0	12.1	0.2	0.2
MD-Informant x med. cond. (less than two med. cond. [a] versus two or more)	108	0.2	0.0	4.4	1.1	1.2
MD-Informant x medications (not taken [a] versus taken meds)	107	4.1	0.1	147.5	0.6	0.6

[a] Reference category

MD-Doc and the MD-Informant. The Wald statistics and -2LL changes for these interactions are not significant, indicating no moderating effects of examined variables.

Research Question 3

Research question 3 seeks to ascertain whether the association between informant reports and physician reports of major depression, and the association between informant reports and subject self-reports of major depression, are moderated by informant characteristics. Table 19 summarizes demographic characteristics of subjects. This table indicates that all informant characteristics at the MD visit were missing on more than 20% of the sample (most were missing on more than 75%), thus precluding any tests for moderation by informant characteristics on any of the three MD visit comparisons. At the CA visit, informant characteristics were likewise missing on more than 20% of the sample for all but the following: informant gender, informant relationship and informant frequency of contact. However, as regards the "sparse cell" problem, the test for moderating effect of informant gender was not possible due to sparse cells in the 3-way table (see Table B31 in Appendix B), thus limiting tests for moderation by informant characteristics to only informant relationship and informant frequency of contact for the one comparison at the CA visit. Thus, the only informant characteristics that could be examined were informant relationship and informant frequency of contact at the CA visit.

CA-Self Versus CA-Informant

Table 20 reports results from informant moderators tested in the CA-SELF versus CA-Informant source comparison. The Wald and -2LL change statistics are not

Table 19

Demographic Summary of Informants

	CA visit		MD visit[a]	
Informant variables	*n*	%	*n*	%
Informant relationship				
Spouse	653	44.1	18	12.2
Non-spouse	681	46	16	10.8
Missing	147	9.9	114	77
Informant frequency of contact				
Lives w/ subject	717	48.4	9	6.1
Not lives w/ subject	537	36.3	3	2
Missing	227	15.3	136	91.9
Informant age				
Less than 65 years old	253	17.1	11	7.4
65+ years old	743	50.2	20	13.5
Missing	485	32.7	117	79.1
Informant gender				
Males	400	27	3	2
Females	937	63.3	11	7.4
Missing	144	9.7	134	90.5
Years Informant known subject				
Less than 55 years	541	36.5	9	6.1
55+ years	550	37.1	14	9.5
Missing	390	26.3	125	84.5

[a] Based on the total number of persons that took either the PCR or GDS at the MD visit

Table 20

CA-Self Regressed on CA-Informant: Informant Moderators

Variable	*n* size	*OR*	95% CI of OR		Wald	-2LL change
CA-Informant[b] x CA visit informant relationship (spouse[a] versus non-spouse)	1,222	1.0	0.2	4.4	0.0	0.0
CA-Informant x CA visit inf. freq. of contact (lives w/ subject[a] versus not lives w/)	1,151	1.2	0.3	5.2	0.1	0.1

[a] Reference category
[b] NPI= Neuropsychiatric Inventory

significant for any of the moderators. These results indicate that agreement between the informant and other sources is moderated by none of the informant characteristics tested.

CHAPTER V

DISCUSSION

This study estimated the extent to which information from physicians' assessments of geriatric depression could be predicted by subjects' assessments and informants' assessments of geriatric depression, and the extent to which informants' assessments and subjects' assessments of geriatric depression could predict each other. Results indicated that, overall, CCMS agreement was best between informants and physicians. These sources agreed fairly well, with informants being slightly more likely to report depression than physicians. Agreement between subjects and both informants and physicians was poor, with subjects being more likely to report depression than the other sources.

Poor agreement on some comparisons may have occurred because different measures were used for different sources. Previous studies provide mixed support for this. For instance, one previous study (McAvay et al., 2005) that used the same measure—The Structured Clinical Interview for Axis I DSM-IV Disorders—with subjects and informants found fair to moderate agreement between subjects and informants on psychological symptoms of depression (diminished interest or pleasure, depressed mood, worthlessness, inappropriate guilt), suicidal symptoms of depression (thoughts of death, suicidal ideation), and somatic symptoms of depression (decreased appetite or weight loss, increased appetite or weight gain, psychomotor agitation or psychomotor retardation, insomnia or hypersomnia, fatigue or loss of energy) (psychological: κ =.41, suicidal: κ =.41, somatic: κ =.31). However, this study also found

poor agreement on cognitive symptoms (indecisiveness or diminished ability to concentrate or think; κ =.09). In addition, Ott and Fogel (1992) found that agreement between sources to be high despite the fact that they used different measures. In this study, caregivers and clinicians agreed quite well (r = 0.92), and subjects and clinicians agreed moderately well (r = 0.40), despite the fact that subjects, caregivers, and clinicians used different measures (the GDS, the HAM-D), and the Cornell Depression Scale for Depression in Dementia, respectively). However, the latter two of these three measures are different measures than those used in the present study.

Differences between this and previous studies may also have occurred because subjects in the Cache County Study on Memory and Health in Aging are different in some regards than participants in previous studies. For instance, subjects in the CA and MD samples had a mean age of 83.0 years (SD = 5.3) and 85.1 years (SD = 5.8), while participants in previous studies had mean ages that ranged from 74 to 78. This could account for lower agreement found in this study, since younger subjects tend to be less concerned about stigma related to reporting depression, thus increasing the likelihood that they will report symptoms. In general, prevalence of depression was higher in this study than in previous studies that assessed prevalence of depression among the elderly. In this study, the percentage of persons having major depression ranged from 4.4% on the CA-Informant to 23.% on the MD-Self, whereas in previous studies the percentage of persons having major depression ranged from 0.86% to 9.4% (Beekman et al., 1995; Djernes, 2006; Eaton et al., 2007; Steffens et al., 2000). This higher prevalence may have occurred because subjects in this study were older than subjects in previous studies. Ethnic

composition was also different in this study; 99.1% of participants in the CA sample were White, whereas 83.9% and 88% of participants in McAvay and colleagues' (2005) study and Snow and colleagues' study (2005), respectively, were White. It is unclear what difference this could have made in agreement. In addition, the religious composition at the CA sample consisted mostly of LDS persons (91.6%), which may have affected agreement. Participants in the CA sample were similar to participants in previous studies in terms of gender composition and education.

This study and previous studies may also have differed because of differences in samples used. Whereas previous studies used participants from clinical samples or participants receiving medical home care services, the present study used a population. This makes participants in the Cache County Study more representative of persons in the U.S. population in general. Subjects and informants that acquire services from clinics tend to be different from those in the general population. For instance, Kokmen, Özsarfati, Beard, O'Brien, and Rocca (1996) found that persons in a clinic-based sample of elderly persons were more likely to be married, to be white collar workers, and to be highly educated than persons in a population-based sample of elderly persons. Those with higher education and occupational status are more likely to have educated beliefs about mental illness, which makes them more likely to report symptoms of depression. Thus, the population-based sample of participants in the Cache County Study is generally more representative of persons in the U.S. population in general, at least insofar as bias due to self-selection to use medical services is concerned. Agreement on depression assessment may be higher among individuals in the subpopulation who seek medical attention. This

may be particularly true when seeking medical care for depressive symptoms, as this behavior likely stems from higher levels of awareness on the part of subject and informant regarding depressive symptoms, perhaps also enhanced by discussion between subject and family members concerning subject's depression, when seeking medical care.

Another key factor that may play a role in this study having relatively poor agreement between subjects and informant ratings is that different measures were used with subjects and informants to assess depression. One way in which depression measures differed is in the length of time over which symptoms were inquired. For instance, the CA-Informant inquires about symptoms in the previous month, while the CA-Self inquires about symptoms over the previous 2 weeks. This may have caused informants to be more likely to report symptoms than the subject. However, in this study subjects reported depression on the CA-Self more often than on the CA-Informant, indicating that subjects reported more depression net of these differences. This suggests that differences between the CA-Self and CA-Informant are due not only to differences in the length of time over which symptoms were inquired, but also to differences between sources.

These measures also differed in that informants are given all of the items on the CA-Informant only if they respond affirmatively on the gateway question, "In the last month, did (NAME) seem sad or depressed? Does (NAME) say that (HE/SHE) feels sad or depressed?" Some older adults manifest depression but without the hallmark symptom of sadness (Gallo & Rabins, 1999). In such cases, informants may still have endorsed enough of the individual items to constitute a diagnosis of major depression disorder.

Thus, it is possible that on this measure depression is less likely to be endorsed than on other measures, such as the CA-SELF. However, if differences between subject reports of depression (as measured by the MD-Self and CA-SELF) and CA-Informant or MD-Informant informant reports of depression were due primarily to the decreased likelihood of depression endorsement on the CA-Informant or MD-Informant due to the gateway question, one would still expect that subjects that were rated as depressed on the CA-Informant or MD-Informant would be also rated as depressed on the MD-Self or CA-Self. Tables 5 and 6 suggest otherwise. Table 5 indicates that only 11 out of the 54 persons diagnosed as depressed on the CA-Informant were diagnosed as depressed on the CA-Self, and Table 6 indicates that only 5 out of 14 persons diagnosed as depressed on the MD-Informant were diagnosed as depressed on the MD-Self, which indicates that disagreement between subjects and informants is not due exclusively to the decreased likelihood of depression endorsement on the CA-Informant or MD-Informant due to the gateway question, but also to differences between sources.

Disagreement between sources may also be due to differences between items on the depression measures. Table 21 explores this possibility. This table compares symptoms queried in the MD-Self, CA-Self, and NPI and compares these measures to DSM-IV criteria for major depression. This table indicates that the MD-Self has more items on depressed mood than the CA-Informant. However, because the MD-Self as a whole has twice as many items as the NPI (assuming that participants answer all items), the number of items addressing depressed mood on the MD-Self is not proportionately larger than number of items on the NPI. Table 21 also indicates that the MD-Self has

Table 21

Comparison of Depression Items

DSM-IV criteria for major depression	MD-Self	NPI	CA-Self
Depressed mood	7. Are you in good spirits most of the time?	3. Sad or in low spirits	
	25. Do you frequently feel like crying?	2. Tearfulness or sobbing	
	16. Do you often feel downhearted and blue?	Seemed sad or depressed (gateway question)	2. Feeling down, depressed, or hopeless
	9. Do you feel happy most of the time?		
	15. Do you think it is wonderful to be alive now?		
	1. Are you basically satisfied with your life?		
Diminished interest or pleasure	2. Have you dropped many of your activities and interests?		1. Little interest or pleasure in doing things
	12. Do you prefer to stay at home, rather than going out and doing new things?		
	19. Do you find life very exciting?		
Weight loss or weight gain			6 & 7. Poor appetite/ overeating
Insomnia or hypersomnia	27. Do you enjoy getting up in the morning?		3 & 4. Trouble falling asleep or staying asleep/sleeping too much
Psychomotor agitation or retardation	11. Do you often get restless and fidgety?	5. Irritable	10 & 11. Moving or speaking slowly/ fidgety and restless
Fatigue or loss of energy	21. Do you feel full of energy?		
Feelings of worthlessness or excessive or inappropriate guilt	3. Do you feel that your life is empty?	11. Says life is not worthwhile	
	17. Do you feel pretty worthless the way you are now?	13. Feels worthless	
		8. Puts self down, feels like a failure	8. Feeling bad about self/that they are a failure/let family down
		9. Says they're a bad person, deserves to be punished	
		12. Says family would be better off without him/her	

(*table continues*)

DSM-IV criteria for major depression	MD-Self	NPI	CA-Self
Diminished ability to think or concentrate, or indecisiveness	26. Do you have trouble concentrating?		9. Trouble concentrating
	14. Do you feel you have more problems with memory than most?		
	6. Are you bothered by thoughts you can't get out of your head?		
	29. Is it easy for you to make decisions?		
	30. Is your mind as clear as it used to be?		
Recurrent thoughts of death, suicidal ideation, suicide attempt/plan		14. Wishes for death, talks about killing self	12. Thinks they are better off dead/thoughts about hurting self
		15. Tried to commit suicide	
Distress, problems in social/ occupational functioning	20. Is it hard for you to get started on new projects?		
	28. Do you prefer to avoid social gatherings?		
Other symptoms			
Helplessness/ hopelessness	5. Are you hopeful about the future?	10. Discouraged, says they have no future	
	10. Do you often feel helpless?		
	22. Do you feel that your situation is hopeless?		
Worry	8. Are you afraid that something bad is going to happen to you?		
	13. Do you frequently worry about the future?		
	18. Do you worry a lot about the past?		
Other	4. Do you often get bored?		
	23. Do you think that most people are better off than you are?		
	24. Do you frequently get upset over little things?		
		1. Currently being treated for depression	
		7. Mood changes a lot	

items that address criteria that the NPI does not address, such as insomnia or hypersomnia, fatigue or loss of energy, lack of concentration or indecisiveness, and distress or problems in social or occupational functioning, indicating that the MD-Self addresses a broader range of criteria than the NPI does. This gave subjects a broader range of symptoms to endorse, which may have increased the likelihood that subjects endorsed enough symptoms to render a diagnosis of depression. The MD-Self also contains items that, if not endorsed, indicate depression. For instance, one of the items states, "Do you feel happy most of the time?" and another states, "Do you enjoy getting up in the morning?" If subjects do not endorse items such as these, one point is added to their score. Because these items are not as directly related to depression, subjects that do not have depression may be more likely to not endorse them, which would increase their total score, making it more likely that their total scores exceeds the threshold for major depression. In addition, the MD-Self contains items that elderly persons would endorse even if they weren't depressed, such as "Have you dropped many of your activities and interests?," "Do you prefer to stay at home, rather than going out and doing new things?," "Do you find live very exciting?," and "Do you feel full of energy?." Items such as these make it more likely that elderly persons who are not depressed exceed the threshold for major depression.

The effect of differences between the CA-Self and CA-Informant on agreement between sources is equivocal. Although the CA-Self addresses criteria that the CA-Informant does not (diminished interest or pleasure, and insomnia or hypersomia) and thus addresses a broader array of symptoms, the CA-Informant has proportionately more

items addressing feelings of worthlessness or excessive or inappropriate guilt, and thus addresses this criterion in more depth. It is unclear how these differences would cause disagreement between these sources.

Poor association between depression reports may also have been due to various statistical issues. For instance, poor association between subject reports of depression and physician and informant reports of depression, relative to the higher association between informants and physicians, may have occurred because only eleven subjects were diagnosed as depressed on the MD-Doc, and of these, only nine were used in analyses. This reduces statistical power to detect associations. However, informants and physicians agreed moderately well despite the low number of persons diagnosed as depressed on the MD-Doc, and subjects and informants on the CA-Self and CA-Informant, respectively, agreed poorly, despite the large number of persons diagnosed as depressed on these measures (115 and 63), indicating that the relatively lower association between subject reports and physician and informant reports of depression, relative to the higher association between informant reports and physician reports, was only partly due to this sample size issue. Also, poor association between depression reports may have occurred because I dichotomized depression reports into major depression versus not major depression. This decreases power to detect associations because it ignores information about differences between persons in the same group (MacCallum, Zhang, Preacher, & Rucker, 2002). For example, an alternative coding of "any depression" versus "no depression" would have resulted in the former group having higher frequency (and therefore higher power).

Similar to this study, previous studies found agreement between sources to be unaffected by most subject and informant characteristics. For instance, McAvay and colleagues (2005) found agreement between sources to be unaffected by subject gender, informant gender, and informant frequency of contact, although they also found that younger informants reported more psychological and cognitive symptoms than older informants. Snow and colleagues (2005) found that physical illness, functional status and caregiver burden did not predict discrepancies between subject and informant reports of depression, and between subject and clinician reports of depression. Similarly, Ott and Fogel (1992) found that history of depression, age, sex, and education could not predict discrepancies between self-reports and clinician reports.

However, also similar to the present study, previous studies found that cognitive impairment is associated with lower agreement between sources. For instance, McAvay and colleagues (2005) found that agreement between cognitively impaired subjects and their informants on the cognitive symptoms of depression (indecisiveness or diminished ability to concentrate or think) was lower than agreement on these symptoms among cognitively normal persons and their informants. Snow and colleagues (2005) found that among persons with a previous diagnosis of dementia, awareness of dementia predicted discrepancies between subject and informant reports of depression, and between subject and clinician reports of depression. Ott and Fogel (1992) found that the correlation between subject and clinician reports of depression was lower among subjects with cognitive impairment. Teri and Wagner (1991) found that dementia severity did not affect agreement. However, this may have occurred because all of the persons in their

sample had AD; although dementia severity can vary among persons with AD, range of dementia severity varies less widely among these persons than among the entire range of not demented versus demented persons. Having only persons with AD would restrict range thereby limiting power to observe effects of dementia severity.

This study has found that other informant and subject characteristics did not affect agreement between sources. This is surprising given previous findings (summarized in Chapter II) regarding these characteristics; that older persons are more likely to associate stigma with depression (Roeloffs et al., 2003), that older males with major depression are less likely to seek treatment (antidepressants and psychotherapy) than older females with major depression (Hinton et al., 2006), and so forth. These findings may have differed from this study because subjects were younger in previous studies. However, some studies were missing specific age information. For instance, Roeloffs and colleagues reported only that the age of participants in their sample ranged from 18 to 90 years and that 55.7% of their sample was older than 41 years old. Hinton and colleagues, who did report specific age information, subject age was comparable to this study; 41.7% of participants in Hinton and colleagues' study were 65-74 years old, and 35.21% of participants study were 75 and older.

Limitations

Some limitations to the present study can be noted. This study analyzed agreement between sources using different measures for each source. This to some extent confounds conclusions regarding the strength of agreement between sources.

Unfortunately, some analyses in this study were precluded by scarce data on informant characteristics. Also, because the main focus of the MD visit was to diagnose dementia, physicians may not have dedicated as much time to diagnosing depression as they would have if their main focus had been diagnosing depression. Further, this study's physician visit comparisons were limited because no cognitively normal subjects were included and the MD visit. Thus, because study physicians understood that the study protocol only selected subjects for this visit who were initially diagnosed with dementia or subsyndromal AD, they may have tended to discount subject's self-report, placing more emphasis on informant report than on the cognitively impaired subject's report.

Strengths

This study had the advantage of utilizing population-level data, which increases representativeness. Also, this study is unique in that it included a higher proportion of individuals in the oldest-old group (aged 85 and older), providing insights into depression assessment in this group not included in many studies. In addition, this study utilized a cognitive status moderator that consisted of an in-depth dementia ascertainment protocol, instead of a simple cognitive screening test used in some studies.

Clinical and Scientific Relevance

Findings from this study help clarify uncertainties regarding the diagnosis of depression in late-life. This information can be valuable to clinicians in their work with elderly persons, in that it could help them identify conditions under which subjects differ

the most from informants and physicians (i.e., subjects differ the most when they have mild cognitive impairment and when they are demented). In addition, this information is invaluable to epidemiologic researchers who study dementia and depression. Finding presented in this study elucidate the strengths and shortcoming of various rating sources of depression, and underscores the importance of carefully selecting depression measures when diagnosing depression among the elderly. Findings from this study also underscore the importance of triangulation in assessing depression among this population, particularly when the subject has notable cognitive impairment.

Future Directions

Because this and previous research indicates that agreement is higher between the informant and physician, future research should further explore informant moderators associated with higher agreement with the physician, with the goal of finding strata of informant characteristics most highly associated with agreement with the physician, to profile "the ideal informant." In addition, future research should be focused on becoming more aware of differences between studies using clinic-based data and those using population-based data in findings regarding rating sources of late-life depression. Finally, qualitative studies may be an important way to understand the phenomenology of depression in late life and what factors influence informants and older adults to feel comfortable disclosing (and even to be aware of) depression.

Summary

This study found agreement in late-life depression to be highest among informants and physicians. Agreement in late-life depression among subjects and both informants and physicians was found to be poor. This agreement was worse than that found in previous studies. However, because this study examined age groups older than those used in previous studies, differences in findings in this study likely reflect unique phenomena among the oldest old. In addition, because this study utilized population-based data while previous studies used clinical-based data, differences in this study may also reflect a more representative view of the U.S. population. Poor agreement on some comparisons occurred in part because different measures were used for different sources. However, this study elucidates differences between these measures that may account for differences in agreement.

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APPENDICES

Appendix A

Physician's Clinical Evaluation of Depression

Cache County Study on Memory Health and Aging
Physician's Clinical Impression of Depressive Disorder

Subject ID#: _____ Date of visit: _____

Physician ID#: _____

Physician is to select one of the following codes that most closely corresponds to his/her clinical impression of the presence of depressive disorder in the participant at the time of the MD visit. This impression is not intended to be a clinical diagnosis or an assessment of whether or not the participant meets explicit DSM algorithmic criteria, and does not assume a complete psychiatric evaluation has been conducted. Rather, it is the physician's overall clinical impression for the purposes of assigning a "working research diagnosis." This diagnosis is determined through information gathered from the subject directly and the collateral informant, including the Geriatric Depression Scale which is self-administered by the subject (Criteria are listed below only as a guide.)

____ (100) no current depression

____ (200) current major depressive episode

____ (300) current minor depressive episode

____ (400) mood disorder NOS

____ (500) bipolar disorder

Major Depressive Episode

In the same 2 weeks, the patient has had 5 or more of the following symptoms, which are a definite change from usual functioning. Either depressed mood or decreased interest or pleasure must be one of the five.

1. Mood. For most of nearly every day, the patient reports depressed mood or appears depressed to others.
2. Interests. For most of nearly every day, interest or pleasure is markedly decreased in nearly all activities (noted by the patient or by others).
3. Eating and weight. Although not dieting, there is a marked loss or gain of weight (such as five percent in one month) or appetite is markedly decreased or increased nearly every day.
4. Sleep. Nearly every day the patient sleeps excessively or not enough.
5. Motor activity. Nearly every day others can see that the patient's activity is agitated or retarded.
6. Fatigue. Nearly every day there is fatigue or loss of energy.
7. Self-worth. Nearly every day the patient feels worthless or inappropriately guilty. These feelings are not just about being sick; they may be delusional.
8. Concentration. Noted by the patient or by others, nearly every day the

patient is indecisive or has trouble thinking or concentrating.

9. Death. The patient has had repeated thoughts about death (other than the fear of dying), suicide (with or without a plan) or has made a suicide attempt.

Additional criteria:

- These symptoms cause clinically important distress or impair work, social or personal functioning.
- They don't fulfill criteria for Mixed Episode.
- This disorder is not directly caused by a general medical condition or the use of substances, including prescription medications.
- Unless the symptoms are severe (defined as severely impaired functioning, severe preoccupation with worthlessness, ideas of suicide, delusions or hallucinations or psychomotor retardation), the episode has not begun within two months of the loss of a loved one.

Minor Depressive Episode

The symptom features and duration are identical to that of major depressive episode with the exception that fewer symptoms are needed to meet diagnostic criteria (2 out of 9 with 1 of the 2 being depressed mood or loss of interest or pleasure). Exclusionary criteria include a past episode of major depression or dysthymia. In addition, the significant distress or impairment criterion found in major depression has been omitted.

Bipolar Disorder

Bipolar disorder has a clinical course that is characterized by the occurrence of one or more Manic episodes or Mixed episodes. Often individuals have also had one or more Major Depressive episodes. Episodes of Substance-induced Mood Disorder or of Mood Disorder Due to a General Medical Condition do not count toward a diagnosis of Bipolar I Disorder.

Mood Disorder NOS

This category includes disorders with mood symptoms that do not meet the criteria for any specific mood disorder and in which it is difficult to choose between Depressive Disorder NOS and Bipolar Disorder NOS.

Appendix B

Supplementary Investigations

SUPPLEMENTARY INVESTIGATIONS

This section describes supplementary descriptive statistics and analyses. These descriptions proceed in the order in which they were originally mentioned in this study. First, I describe the process by which I selected cases from Waves 3 and 4, and then report analyses assessing the equivalence on a number of demographic factors of participants taken from these time points. I then describe the mean imputation procedure I used for the CA-Self. Next, I describe the process by which I determined multicollinearity between informant relationship and number of years the informant had known the subject. Finally, I include tables reporting cell size for models that included moderator variables.

Selecting Between Waves 3 and Wave 4

To ensure independence of observations, I used subjects' data from only one wave. I used Wave 3 data if the subject completed Wave 3. Otherwise, I used Wave 4 data. This protocol was followed separately for CA and MD visit, such that if a subject had CA in both Waves 3 and 4, but MD visit only in Wave 4, then Wave 3 CA data and Wave 4 MD visit data were used for that subject. The total number of participants used for each measure overall and within each wave, are listed in Table B1. The MD-Doc and MD-Self were added mid-way through Wave 3 fieldwork. Because of this, only 127 of the 357 persons that participated in Wave 3 were given these measures, and of these, 124 completed the MD-Doc and 112 completed the MD-Self.

Table B1

Number of Persons from Each Wave

Participant	Wave 3 used	Wave 4 used	Total
CA-Informant	1,203	243	1,446
PHQ_9	1,135	238	1,373
MD-Informant	279	20	299
MD-Self	112	24	136
MD-Doc	124	24	148
subject dementia status	1,228	252	1,480
CA visit subject age	1,226	252	1,478
MD visit subject age	357	25	382
medications	1,228	252	1,480
CA visit informant rel. to subject	1,087	247	1,334
CA visit informant freq. of contact	1,039	215	1,254
CA visit informant age	756	240	996
CA visit informant gender	1,090	247	1,337
CA visit years informant known subject	861	230	1,091
MD visit informant rel. to subject	45	19	64
MD visit informant frequency of contact	41	0	41
MD visit informant age	39	19	58
MD visit informant gender	44	0	44
MD visit years informant known subj.	35	12	47

Equivalence of Waves 3 and 4 on Demographic Factors

To determine equivalence across a range of demographic variables between subjects whose data were from Wave 3 versus from Wave 4, chi-square tests of independence were conducted (see Table B2). As can be seen, the CA and MD-Informant, MD-Self, MD-Doc, MD visit subject age, CA visit informant relationship to subject, CA visit informant frequency of contact, CA visit informant gender, CA visit years the informant had known subject, MD visit informant relationship to subject, MD visit informant frequency of contact, MD visit informant age, and MD visit years the

Table B2

Wave 3 and Wave 4 Differences

Category	Chi square	*p* value
CA-Informant (major dep vs no major dep)	0.2	0.63
PHQ 9-CA (major dep vs no major dep)	5.4	0.02
MD-Informant (major dep vs no major dep)	2.5	0.11
MD-Self (major dep vs no major dep)	0.5	0.47
MD-Doc (major dep vs no major dep)	0.0	0.85
subject dementia (normal, MCI/OCI, dementia)	7.9	0.02
CA visit subject age (<85 versus 85+ yrs. old)	11.3	0.00
MD visit subject age (<85 versus 85+ yrs. old)	0.4	0.54
medications (meds taken versus not taken)	7.8	0.01
CA visit informant rel. to subject (spouse versus non-spouse)	3.3	0.07
CA visit informant freq. Of contact (lives with subj vs not lives with)	0.0	0.89
CA visit informant age (<65 versus 65+ yrs. old)	35.6	<.001
CA visit informant gender	1.6	0.21
CA visit years informant known subj. (<55 versus 55+ yrs.)	5.0	0.03
MD visit informant rel. to subject (spouse versus non-spouse)	0.4	0.51
MD visit informant freq. Of contact (lives with subj vs not lives with)	*	*
MD visit informant age (<65 versus 65+ yrs. old)	0.0	0.94
MD visit informant gender	*	*
MD visit years informant known subj. (<55 versus 55+ yrs.)	0.1	0.78

informant had known subject were nonsignificant, indicating that Wave 3 participants were the same as Wave 4 participants on these factors.

Conversely, Wave 3 and Wave 4 subjects were found to differ on cognitive status- Wave 4 subjects were less likely to be MCI/OCI or demented than Wave 3 subjects. The may be due to the method by which I decided which wave to use for each subject, described previously. Subjects for whom I used Wave 4 data were subjects who did not pass the cognitive screen and were thus less cognitively impaired at Wave 3 than subjects

for whom I used Wave 3 data. This may explain why they were still less cognitively impaired at Wave 4 than Wave 3 subjects. It was also found that subjects at the Wave 3 CA visit were more likely to be 85 years of age or older (versus less than 85 years of age) than subjects at the Wave 4 CA visit. The may also be due to the method of deciding which wave to use; Wave 4 subjects did not pass the cognitive screen and were thus less cognitively impaired at Wave 3 than Wave 3 subjects, which implies that they were younger at Wave 3 than Wave 3 subjects, young enough that they may have still been younger at Wave 4 than Wave 3 subjects at Wave 3. I also found that Wave 4 CA informants were more likely to have known the subject for more than 55 years (versus less than 55 years), which is logical, given an additional 3 years elapsed between waves. In addition, Wave 4 subjects were more likely to use medication with depressogenic side effects than Wave 3 subjects. This is surprising, given the previous finding that Wave 4 subjects were younger than Wave 3 subjects. I also found that Wave 4 CA informants were more likely to be less than 65 years of age than Wave 3 CA informants. This may be because Wave 4 CA informants were slightly less likely to be spouses than Wave 3 CA informants (this difference approached significance—$\chi^2 = 3.3$, $p = .07$), and CA spouse informants were more likely to be 65 and older than CA non-spouse informants ($\chi^2 = 510.9$, $p < .001$). I also found that Wave 4 subjects were more likely to be depressed on the CA-Self than Wave 3 subjects, and that Wave 3 subjects had a longer elapsed time between CA and MD visit than Wave 4 subjects; mean elapsed time was 8.1 months ($SD = 5.6$) for Wave 3 subjects and 6.6 months ($SD = 2.9$) for Wave 4 subjects ($p = .031$). It is unclear why these results would occur.

Mean Imputation Procedure for PHQ-9

If a subject had any missing responses on the CA-Self, I added to the total score the mean of the nonmissing responses for each item that was missing, provided that no more than four items were missing. This method of mean substitution differs from that in which the mean total score of participants with non-missing total scores is imputed as the mean total score for participants with missing total scores. The latter method has been discredited because it biases scores towards the average (Graham, 2009). In this study, the mean of each participant's non-missing items is imputed as the value for their missing items, resulting in a more personally tailored estimate of each participant's total score. Of the 1,481 persons that went to the CA visit, 107 did not complete the CA-Self or were missing more than four items, 1,362 completed the entire CA-Self, and 11 completed the CA-Self but had four or fewer items missing. Of this latter group, an average of 0.79 points (range: 0.25 to 1.60) was imputed to each score. This imputation resulted in two cases moving from not having major depression to having major depression.

Analyses were conducted to assess the equivalence on a number of demographic characteristics, as well as on cognitive status, across those who did not complete the CA-Self (or were missing more than four items), those who completed the entire CA-Self, and those who completed the CA-Self but had four or fewer items missing, i.e., those that received the mean imputation. I used ANOVA to assess equivalence across these missingness groups on years of education and subject age at the CA visit. Omnibus ANOVA was significant for years of education, $F(2,1469) = 3.9$, $p = .02$. Post hoc Tukey tests revealed that those who did not complete the CA-Self had significantly fewer years

of education (M = 12.9) than those who completed the entire CA-Self (M = 13.7). The mean of the mean imputation group (M = 13.5) was similar to the completed group, but was not significantly different from the non-completed group, most likely because of low cell size. Omnibus ANOVA was also significant for subject age, $F(2, 1477) = 22.00$, $p < .001$. Similar to years of education, post hoc Tukey tests revealed that the noncompleted group was significantly older (M = 86.2) than the completed group (M = 82.7), with the mean imputation group being equivalent to the completed group (M = 82.7). These analyses indicate that participants who received the mean imputation were similar to those who completed the entire CA-Self in terms of age and education, and that these two groups were different from those that did not complete the CA-Self in terms of these factors.

Table B3 presents results from chi-square analyses that assess equivalence across missingness groups on the remaining demographic factors and on cognitive status. Ethnicity, marital status, and gender were not significant, indicating that participants in the different missingness groups were similar on these factors. The chi square test for cognitive status was significant, χ^2 (4, n = 1,480) = 60.8, $p < .001$. Crosstabulations

Table B3

Equivalence Across Missingness Categories on PHQ-9

Category	Chi square	*p* value
Ethnicity	11.4	0.08
Marital status	12.2	0.14
Gender	3.6	0.17
Cognitive status	60.8	< .0005

indicated that those who did not complete the CA-Self (n = 107) were more likely to be demented than those who did complete the CA-Self (n = 1,362) and those who received the mean imputation (n = 11). This increased likelihood of dementia may explain why these subjects could not complete all or some items on this measure, despite being similar to subjects who completed the measure in terms of age and education.

Determining Multicollinearity Between Informant Relationship and Number of Years the Informant Had Known the Subject

To assess the possibility that the informant relationship with the subject and the number of years the informant had known the subject were the same construct, I computed Pearson correlations between these factors. Because spouses were coded as "1" and nonspouses were coded as "2," a negative relationship would indicate that spouse informants were more likely to have known the subject for longer. This correlations was low (CA visit: r = -.221, MD visit: r = -.394), indicating that, although the constructs are similar and overlap, they are dissimilar enough to consider them separately as potential moderator variables influencing agreement on pairs of depression measures.

Tables Reporting Cell Sizes for Models that Included Moderators

Tables B4-B32 report cell sizes for models that included moderators.

Table B4

CA-Self by CA-Informant and Subject Gender

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
Male	524	93.4	37	6.6	561
Female	673	91.4	63	8.6	736
Major depression					
Male	24	82.8	5	17.2	29
Female	19	76.0	6	24.0	25
Total	1,240		111		1,351

Table B5

CA-Self by CA-Informant and Subject Age

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
< 85	797	92.7	63	7.3	860
85+	398	91.5	37	8.5	435
Major depression					
< 85	29	74.4	10	25.6	39
85+	14	93.3	1	6.7	15
Total	1,238		101		1,339

Table B6

CA-Self by CA-Informant and Dementia

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
Normal	567	97.3	16	2.7	583
MCI/OCI	492	88.0	67	12.0	559
Dementia	138	89.0	17	11.0	155
Major depression					
Normal	7	77.8	2	22.2	9
MCI/OCI	18	85.7	3	14.3	21
Dementia	18	75.0	6	25.0	24
Total	1,240		111	1	1,351

Table B7

CA-Self by CA-Informant and Subject Prior History of Depression

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
No prior major depression	1,012	94.8	55	5.2	1,067
Prior major depression	148	79.1	39	20.9	187
Major depression					
No prior major depression	29	85.3	5	14.7	34
Prior major depression	12	66.7	6	33.3	18
Total	1,201		103		1,304

Table B8

CA-Self by CA-Informant and Subject Medical Conditions

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
Had < 2 medical conditions	466	94.9	25	5.1	491
Had 2+ medical conditions	731	90.7	75	9.3	806
Major depression					
Had < 2 medical conditions	21	91.3	2	8.7	23
Had 2+ medical conditions	22	71.0	9	29.0	31
Total	1,240		111		1,351

Table B9

CA-Self by CA-Informant and Subject Medication Use

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
Not taken meds	932	92.9	71	7.1	1,003
Taken meds	265	90.1	29	9.9	294
Major depression					
Not taken meds.	34	79.1	9	20.9	43
Taken meds.	9	81.8	2	18.2	11
Total	1,240		111		1,351

Table B10

MD-Self by MD-Informant and Subject Gender

	MD-Self				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
Male	35	92.1	3	7.9	38
Female	33	66.0	17	34.0	50
Major depression					
Male	5	71.4	2	28.6	7
Female	4	57.1	3	42.9	7
Total	77		25		102

Table B11

MD-Self by MD-Informant and Subject Age

	MD-Self				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
< 85	41	82.0	9	18.0	50
85+	27	71.1	11	28.9	38
Major depression					
< 85	7	70.0	3	30.0	10
85+	2	50.0	2	50.0	4
Total	77		25		102

Table B12

MD-Self by MD-Informant and Cognitive Status

	MD-Self				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
MCI/OCI	44	75.9	14	24.1	58
Dementia	18	78.3	5	21.7	23
Major depression					
MCI/OCI	3	50.0	3	50.0	6
Dementia	5	71.4	2	28.6	7
Total	70		24		94

Table B13

MD-Self by MD-Informant and Prior History of Depression

	MD-Self				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
No prior major depression	62	82.7	13	17.3	75
Prior major depression	5	50.0	5	50.0	10
Major depression					
No prior major depression	6	66.7	3	33.3	9
Prior major depression	3	75.0	1	25.0	4
Total	76		22		98

Table B14

MD-Self by MD-Informant and Medical Conditions

	MD-Self				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
Had < 2 medical conditions	24	77.4	7	22.6	31
Had 2+ medical conditions	44	77.2	13	22.8	57
Major depression					
Had < 2 medical conditions	3	50.0	3	50.0	6
Had 2+ medical conditions	6	75.0	2	25.0	8
Total	77		25		102

Table B15

MD-Self by MD-Informant and Medications

	MD-Self				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
Not taken meds.	55	78.6	15	21.4	70
Taken meds.	13	72.2	5	27.8	18
Major depression					
Not taken meds.	7	63.6	4	36.4	11
Taken meds.	2	66.7	1	33.3	3
Total	77		25		102

Table B16

MD-Doc by MD-Self and Gender

	MD-Doc				
	No major depression		Major depression		
MD-Self	*n*	%	*n*	%	total
No major depression					
Male	44	95.7	2	4.3	46
Female	55	94.8	3	5.2	58
Major depression					
Male	5	71.4	2	28.6	7
Female	23	92.0	2	8.0	25
Total	127		9		136

Table B17

MD-Doc by MD-Self and Subject Age

	MD-Doc				
	No major depression		Major depression		
MD-Self	*n*	%	MD-Self	*n*	%
No major depression					
< 85	58	92.1	5	7.9	63
85+	41	100.0	0	0.0	41
Major depression					
< 85	11	78.6	3	21.4	14
85+	17	94.4	1	5.6	18
Total	127		9		136

Table B18

MD-Doc by MD-Self and Dementia Status

	MD-Doc				
	No major depression		Major depression		
MD-Self	*n*	%	MD-Self	*n*	%
No major depression					
MCI/OCI	63	95.5	3	4.5	66
Dementia	27	93.1	2	6.9	29
Major depression					
MCI/OCI	19	86.4	3	13.6	22
Dementia	8	88.9	1	11.1	9
Total	127		9		136

Table B19

MD-Doc by MD-Self and Prior History of Depression

	MD-Doc				
	No major depression		Major depression		
MD-Self	*n*	%	*n*	%	total
No major depression					
No prior major depression	86	96.6	3	3.4	89
Prior major depression	11	84.6	2	15.4	13
Major depression					
No prior major depression	19	90.5	2	9.5	21
Prior major depression	7	87.5	1	12.5	8
Total	123		8		131

Table B20

MD-Doc by MD-Self and Medical Conditions

	MD-Doc				
	No major depression		Major depression		
MD-Doc	*n*	%	*n*	%	total
No major depression					
Had < 2 medical conditions	34	91.9	3	8.1	37
Had 2+ medical conditions	65	97.0	2	3.0	67
Major depression					
Had < 2 medical conditions	7	85.7	2	14.3	14
Had 2+ medical conditions	16	88.9	2	11.1	18
Total	127		9		136

Table B21

MD-Doc by MD-Self and Medications

	MD-Doc				
	No major depression		Major depression		
MD-Self	*n*	%	*n*	%	total
No major depression					
Not taken meds.	76	96.2	3	3.8	79
Taken meds.	23	92.0	2	8.0	25
Major depression					
Not taken meds.	22	88.0	3	12.0	25
Taken meds.	6	85.7	1	14.3	7
Total	127		9		136

Table B22

MD-Doc by MD-Informant and Gender

	MD-Doc				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
Male	44	95.2	2	4.8	42
Female	49	96.1	2	3.9	51
Major depression					
Male	4	57.1	3	42.9	7
Female	6	75.0	2	25.0	8
Total	99		9		108

Table B23

MD-Doc by MD-Informant and Subject Age

	MD-Doc				
	No major depression		Major depression		
MD-Informant	*n*	%	MD-Self	*n*	%
No major depression					
< 85	49	92.5	4	7.5	53
85+	40	100.0	0	0.0	40
Major depression					
< 85	6	60.0	4	40.0	10
85+	4	80.0	1	20.0	5
Total	99		9		108

Table B24

MD-Doc by MD-Informant and Cognitive Status

	MD-Doc				
	No major depression		Major depression		
MD-Informant	*n*	%	MD-Self	*n*	%
No major depression					
MCI/OCI	59	95.2	3	4.8	62
Dementia	23	95.8	1	4.2	24
Major depression					
MCI/OCI	3	50.0	3	50.0	6
Dementia	5	71.4	2	28.6	7
Total	90		9		99

Table B25

MD-Doc by MD-Informant and Prior History of Depression

	MD-Doc				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
No prior major depression	76	95.0	4	5.0	80
Prior major depression	10	100.0	0	0.0	10
Major depression					
No prior major depression	8	88.9	1	11.1	9
Prior major depression	2	40.0	3	60.0	5
Total	96		8		104

Table B26

MD-Doc by MD-Informant and Medical Conditions

	MD-Doc				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
Had < 2 medical conditions	31	96.9	1	3.1	32
Had 2+ medical conditions	58	95.1	3	4.9	61
Major depression					
Had < 2 medical conditions	3	50.0	3	50.0	6
Had 2+ medical conditions	7	77.8	2	22.2	9
Total	99		9		108

Table B27

MD-Doc by MD-Informant and Medications

	MD-Doc				
	No major depression		Major depression		
MD-Informant	*n*	%	*n*	%	total
No major depression					
Not taken meds.	71	95.9	3	4.1	74
Taken meds.	18	94.7	1	5.3	19
Major depression					
Not taken meds.	8	72.7	3	27.3	11
Taken meds.	1	33.3	2	66.6	3
Total	98		9		108

Table B28

CA-Self by CA-Informant and Informant Relationship

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
Spouse	555	93.9	36	6.1	591
Non-spouse	523	90.2	57	9.8	580
Major depression					
Spouse	15	83.3	3	16.7	18
Non-spouse	25	75.8	8	24.2	33
Total	1,118		104		1,222

Table B29

CA-Self by CA-Informant and Informant Frequency of Contact

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	*n*	%	total
No major depression					
Lives with subject	601	92.7	47	7.3	648
Not lives subject	416	90.8	42	9.2	458
Major depression					
Lives with subject	16	80.0	4	20.0	20
Not lives subject	18	72.0	7	28.0	25
Total	1,051		100		1,151

Table B30

CA-Self by CA-Informant and Informant Age

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	MD-Self	*n*	%
No major depression					
< 65 years old	197	89.1	24	10.9	221
65+ years old	626	93.0	47	7.0	673
Major depression					
< 65 years old	11	73.3	4	26.7	15
65+ years old	16	88.9	2	11.1	18
Total	850		77		927

Table B31

CA-Self by CA-Informant and Informant Gender

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	MD-Self	*n*	%
No major depression					
Male	329	91.1	32	8.9	361
Female	752	92.5	61	7.5	813
Major depression					
Male	3	100.0	0	0.0	3
Female	37	77.1	11	22.9	48
Total	1,121		104		1,225

Table B32

CA-Self by CA-Informant and Number of Years the Informant Had Known Subject

	CA-Self				
	No major depression		Major depression		
CA-Informant	*n*	%	MD-Self	*n*	%
No major depression					
< 55 years old	427	91.0	42	9.0	469
55+ years old	454	91.5	42	8.5	496
Major depression					
< 55 years old	24	75.0	8	25.0	32
55+ years old	6	85.7	1	14.3	7
Total	911		93		1,004