SECOND-GENERATION ANTIDEPRESSANT USE IN TREATMENT FOR MAJOR DEPRESSIVE DISORDER-AN EXAMINATION OF GUIDELINE COMPONENTS AND HEALTHCARE UTILIZATION

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ABSTRACT

SHIH-YIN CHEN: Second-generation Antidepressant Use in Treatment for Major Depressive Disorder - An Examination of Guideline Components and Healthcare Utilization (Under the direction of Dr. Matthew Maciejewski)

Major depressive disorder (MDD) is a prevalent mental health illness and antidepressant therapy is the most frequently provided treatment option. Clinical guidelines have been developed for depression management. Guidelines recommend that depressed patients receive frequent follow-up visits and complete an acute phase regimen lasting a minimum of 6-8 weeks to remove symptoms, followed by a continuation phase for 4-9 months to prevent relapse. The objectives of this dissertation are to examine whether there are differences between patients initially prescribed an antidepressant by providers with different specialties, to understand what factors are associated with receipt of guideline-concordant care, and investigate how subsequent healthcare utilization varies by provider specialty and guideline concordance.

Claims data from a large national plan in 2000-2004 were used to identify individuals who initiated antidepressant treatment for MDD. Guideline-concordant follow-up visits were identified based on service claims, and completion of acute phase and continuation phase antidepressant regimens was evaluated based on prescription refill records. All-cause and mental health-related hospitalizations and emergency room visits were examined during a

one-ear period after treatment completion. Logistic regressions were conducted to assess the association of the outcomes with initial prescriber specialty and other factors.

We found that several pre-disposing, enabling and need variables differ among patients with different types of providers. After adjustment, patients initially prescribed an antidepressant by psychiatrists were more likely to receive guideline-concordant follow-up visits, and no provider differences were found for antidepressant treatment completion. Patients who received guideline-concordant follow-up visits were more likely to complete antidepressant treatment. Completion of acute phase treatment was negatively associated with all-cause hospitalization during the one-year period afterwards.

These results showed that routine care for antidepressant management falls short of guideline recommendations. These findings underscore the need for quality improvement particular in primary care. Strategies to promote frequent follow-up should be encouraged given the positive association with antidepressant adherence. This study also helps identify the modifiable factors to target for intervention and provides evidence to justify resource allocation to promote quality of care among patients with MDD.

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LIST OF ABBREVIATIONS

AHCPR Agency for Health Care Policy and Research

APA American Psychiatric Association

CCM Chronic Care Model

CDS Chronic Disease Score

CI Confidence Interval

DRG Diagnosis-related Group

HEDIS Healthcare Effectiveness Data and Information Set

ICD-9-CM International Classification of Disease, 9^{th} revision, Clinical Modification

MD Medical Doctor

MDD Major Depressive Disorder

MPR Medication Possession Ratio

NCQA National Committee of Quality Assurance

PCP Primary Care Provider

OR Odds Ratio

SNRI serotonin norepinephrine reuptake inhibitor

SSRI selective serotonin reuptake inhibitor

VA Veteran Administration

CHAPTER I

INTRODUCTION

1.1 Specific Aims

Major depressive disorder (MDD) is a prevalent mental health illness that impacts 32.6 to 35.1 million Americans.[1] Among the available treatment options for MDD, antidepressant therapy is most frequently used because of its easy administration and high effectiveness. The effectiveness of antidepressant therapy relies heavily on patient adherence, which has been estimated to range from 11% to 65%. [2-7]

Clinical practice guidelines, such as the Agency for Health Care Policy and Research (AHCPR) Depression Guideline Panel Report and the practice guideline for treatment of patients with major depression by the American Psychiatric Association (APA), have been developed to assist patients and providers in the treatment of MDD. If pharmacotherapy is chosen, it is recommended that an acute phase regimen lasting a minimum of 6-8 weeks should be completed in order to remove symptoms, followed by a continuation phase for 4-9 months to prevent relapse.[8, 9]

Guidelines also suggest frequent outpatient follow-up visits during the acute phase. Although guidelines have been developed for over a decade, routine primary care management for depression still falls short of guideline recommendations. Only half to two thirds of patients receive care for MDD.[1, 10] Among those seeking healthcare, only one forth received appropriate treatment.[1, 11]

This dissertation seeks to understand the care patients with MDD receive, and the association between initial prescriber specialty, receipt of guideline-concordant outpatient follow-up visits, completion of antidepressant treatment phases and subsequent healthcare utilization. The dissertation used a retrospective cohort of patients with MDD between 2000 and 2004. Medical and pharmacy claims data from a large national healthcare plan affiliated with i3 Innovus were analyzed to address the following aims:

<u>Aim 1</u>: To examine characteristics among patients initially prescribed an antidepressant by providers with different specialties to treat major depressive disorder (MDD)

This aim examines characteristics among patients initially prescribed an antidepressant by providers with different specialties. Information on prescribing provider specialty was obtained from the index antidepressant prescription claim. Patient cohorts were identified based on the specialty of the provider who prescribed the index antidepressant from: 1) a primary care provider; 2) a psychiatrist; or 3) a non-psychiatric specialist. Patient difference by the initial prescriber specialty may indicate potential confounders of the provider effect related to outpatient follow-up, antidepressant treatment completion, and subsequent healthcare utilization. There might be substantial differences in patient characteristics as well as depression outcomes for patients seen by different types of providers, and failure to acknowledge this might mask important differences.

<u>Aim 2:</u> To examine the association of antidepressant treatment with initial prescriber specialty and receipt of guideline-concordant outpatient follow-up visits among patients with MDD

H2.1: Receipt of guideline-concordant outpatient follow-up visits varies by initial prescriber specialty

This aim examines the association between initial prescriber specialty and receipt of guideline-concordant outpatient follow-up visits during acute phase. Receipt of guideline-concordant follow-up visits is defined as having at least three visits during the first 90 days since treatment initiation using the National Committee for Quality Assurance (NCQA) Health Effectiveness Data and Information Set (HEDIS) measure.[12] Prior studies found mental health specialty care were associated with increased likelihood of receipt of guideline-concordant follow-up visits.[4, 6] This dissertation extended prior work by incorporating risk adjustment in the analytical models and propensity score matching to account for imbalance of patient characteristics among provider specialties. Furthermore, we conducted additional sensitivity analyses by varying the approach to identify follow-up visits to evaluate how our results may change based on how we define follow-up visits. The findings from this aim could inform quality improvement by identifying the population at risk of less frequent follow-up and targeting modifiable components for intervention.

H2.2: Completion of antidepressant acute and continuation phase varies by initial prescriber specialty

This aim investigates the association between initial prescriber specialty and antidepressant treatment. Clinical guidelines suggest that a patient should complete an acute phase regimen (6-8 weeks) and a continuation phase treatment (4-9 months).[8, 9] Previous findings about the association between provider specialty and antidepressant treatment were inconsistent. [2-4, 6, 7, 13-17] Further, empirical evidence of the association between receipt of guideline-concordant follow-up visits and antidepressant treatment is needed to demonstrate

whether follow-up visits reinforce patient's completion of antidepressant treatment, but only one study based on a military veterans sample has controlled for provider specialty and follow-up visits simultaneously.[4] This dissertation extends earlier work by incorporating both provider specialty and guideline-concordant follow-up visits in the analytical model, measuring antidepressant use aligned with guideline recommendations, and utilizing propensity score matching to control for confounders. Since suboptimal antidepressant treatment is widespread in real-world practice, it is critical to understand factors associated with patient's antidepressant treatment completion. The knowledge gained from this aim can provide a basis for developing interventions to improve the quality of antidepressant treatment that patients with MDD receive.

<u>Aim 3</u>: To examine the association of subsequent healthcare utilization with initial prescriber specialty and antidepressant treatment among patients with MDD

This aim examines subsequent *all-cause* and *mental health-related emergency room visits and hospitalization* during one-year period after acute phase and continuation phase to understand the relationship with initial prescriber specialty and antidepressant treatment. Even though emergency room visits or hospitalization are rare events, they account for a large portion of healthcare costs and might indicate a clinical exacerbation of the condition. As the majority of depression patients are treated in primary care settings[11], it is important to examine the influence of provider specialty on subsequent emergency room visits and inpatient admissions to understand what the downstream economic implications of treatment by providers with different specialties are. Empirical evidence linking antidepressant treatment duration to economic outcomes is more limited, particularly for hospitalization.[18-20] With increasing prescription drug expenditures, it is important to link antidepressant

treatment duration to subsequent utilization of healthcare to understand potential cost offset effects. If reduction in these costly healthcare events can be attributed to adequate use of medication, costs associated with medication use can be justified both by its cost offset effects as well as the expected improvement in health outcomes. Findings from this analysis can provide empirical evidence to assess the importance of antidepressant treatment with guideline-recommended duration from both clinical and economic perspectives.

1.2 Background of Major Depressive Disorder

1.2.1 Diagnosis

Major depressive disorder (MDD) is a psychiatric mood disturbance characterized by one or more major depressive episodes without a history of manic, mixed, or hypomanic episodes.[21] A major depressive episode is a period of at least two weeks during which there is depressed mood or loss of interest or pleasure in nearly all activities. The criteria for major depressive episode in the Diagnostic and Statistical Manual of Mental Disorders Forth Edition (DSM-IV)[21] are listed in Appendix 1.

The cause of MDD can be idiopathic or related to a wide range of systemic or neurological medical illnesses, substance intoxication or withdrawal. Clinical history and mental status examination are the most important components of the diagnostic evaluation because depressive disorders are defined by syndrome criteria. Although MDD is a common and treatable mood disorder, it is still under-diagnosed. The reasons for under-diagnosis range from lack of screening to denial by patients due to stigma.[22] Depression is also often under-treated. Only half to two thirds of patients with defined MDD receive treatment.[1, 10] Among those who seek care, the majority of MDD patients see primary care providers (78%), while only 18% visited mental health specialists.[11] Only one fourth of those seeking health care receive appropriate treatment.[1, 11]

1.2.2. Epidemiology and Burden of Illness

MDD affects 32.6 to 35.1 million adults in the United States, with higher rates among women[1] (Table 1.1). Mean age at onset of MDD is 30.4 years.[10] There is a 40% rate of recurrence over a two-year period after the first episode.[23] Among those with lifetime MDD, the mean number of episodes was 4.7, and the median duration was 24.3 weeks for the

longest episode.[10] MDD is also commonly comorbid with anxiety and substance disorders.[1, 10]

Table 1.1 Prevalence of Major Depressive Disorder in the United States

Study	Year	Diagnostic Criteria	1-year prevalence	Lifetime prevalence
Robins et al. [24]	1980s	DSM-III	3.0%	5.2%
Kessler et al. [25]	1990-1992	DSM-III-R	8.6%	14.9%
Kessler et al. [1]	2001-2002	DSM-IV	6.6%	16.2%
Hasin et al. [10]	2001-2002	DSM-IV	5.3%	13.2%

The World Health Organization ranked MDD as the most burdensome disease in the world,[26] and projected that depression will be the second leading cause of disability in the developed world by 2020.[27] MDD interferes with functioning in work, household, relationship and social roles, and individuals with 12-month MDD reported a mean of 35.2 days of role impairment.[1] In addition, the economic burden of depression is high. The average annual costs per case ranged from $1,000 to $2,500 in direct healthcare costs, from $2,000 to $3,700 for morbidity costs and from $200 to $400 mortality costs.[28] In the United States, the annual burden of depression was estimated to be $81.5 billion in 2000.[29]

1.2.3 Treatment Options

After a confirmed diagnosis, treatment should be initiated according to clinical need (e.g. severity of symptoms) and patient preferences. Treatment options for MDD include pharmacotherapy, psychotherapy, combination of pharmacotherapy and psychotherapy, and electroconvulsive therapy.

Pharmacotherapy is the most frequently used treatment for MDD, particularly for patients with mild to moderate MDD.[30] It is estimated that 62% of depressed patients are initiated with pharmacotherapy.[31] The major classes of drugs are the selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, heterocyclics, monoamine oxidase inhibitors, and a few other compounds.

Antidepressants are efficacious and associated with a 50-60% response rate among patients in primary care settings.[32] Second-generation antidepressants, including SSRIs and SNRIs, are usually used as the first-line choice in primary care because of their lower side effect profiles and markedly lower risk of overdose.[33] The advantages of pharmacotherapy are easy administration, high effectiveness and low patient time requirement compared with psychotherapy. Some of the disadvantages of pharmacotherapy include need for repeated medical visits to monitor response and adjust dosage, unwanted side effects, and most importantly, failure to complete treatment (e.g. non-adherence).[8]

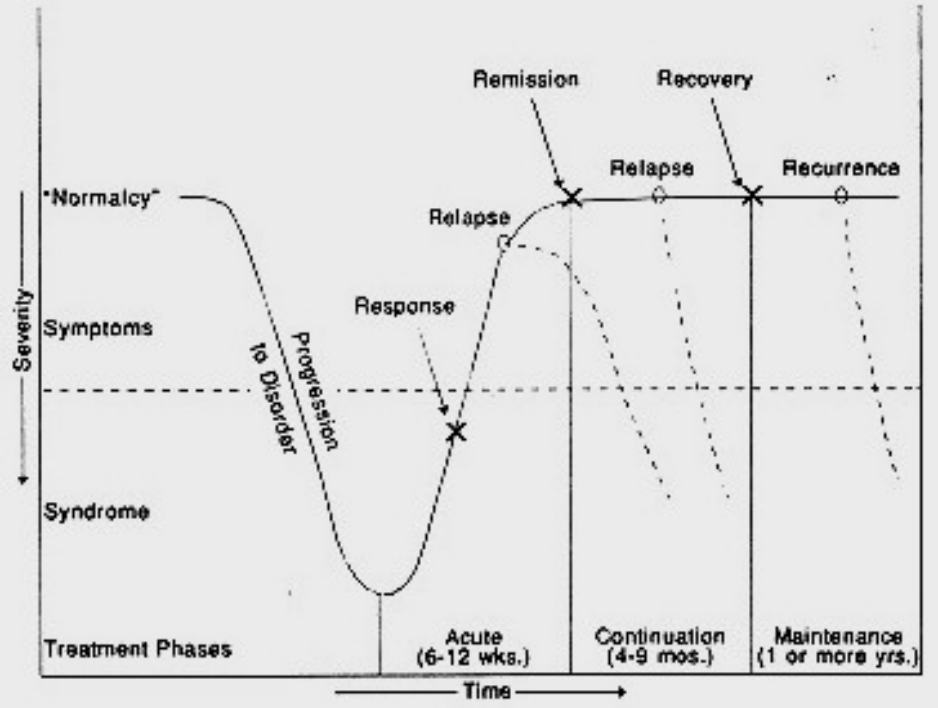
Psychotherapy, such as cognitive therapy, behavioral therapy, and interpersonal therapy, is also effective in treating depression.[34] Cognitive therapies aim at symptom removal by identification and correction of the patient's distorted, negatively biased, moment-to-moment thinking.[35] Behavioral therapies usually involve a functional analysis of behavior and/or social learning. Interpersonal therapies aim at the clarification and resolution of the interpersonal difficulties. Psychotherapy is more time-consuming and expensive than pharmacotherapy, and the treatment effects appear much later.[8] A combination of pharmacotherapy and psychotherapy can be given if either treatment alone is only partially effective, or the clinical circumstances suggest both aspects to be targeted at the same time. [8] Finally, electroconvulsive therapy is only appropriate for patients with severe and/or psychotic depressions who have not responded to other treatment. [8]

1.2.4 Clinical Practice Guidelines for Antidepressant Therapy in Treating Major Depressive Disorder

Clinical practice guidelines such as the Agency for Health Care Policy and Research (AHCPR) Depression Guideline Panel Report[8] and American Psychiatric Association (APA)

Practice Guideline for the Treatment of Patients with Major Depressive Disorder[9] have been developed to assist patients and providers in the treatment of MDD. According to these guidelines, the overall aim of the treatment is the attainment of a stable, fully asymptomatic state and full restoration of psychosocial function (a remission). The treatment phases of MDD are outlined in Figure 1.1 and Table 1.2.

Figure 1.1 Treatment Phases of Major Depressive Disorder



Source: Kupfer DJ. Long-term treatment of depression. J Clin Psychiatrty 1991;52(Suppl 5):28-34.

Once treatment is initiated, the severity of symptoms should decrease if patients respond to the treatment. It is recommended that an acute phase medication regimen lasting a minimum of 6-8 weeks should be completed in order to remove symptoms. The acute phase ends when patients achieve remission. If patients respond to medication during the acute phase, a continuation regimen for another 4 to 9 months with the same medication at the same dosage should be followed to prevent relapse. Patients who have had three or more

episodes of major depression are potential candidates for long-term maintenance antidepressant treatment.

Table 1.2 Treatment Phases of Major Depressive Disorder

	Acute Phase	**Continuation Phase**	**Maintenance Phase**
Duration	6-12 weeks	4-9 months	≥ 1 year
Aim	removing all depressive symptoms	preventing relapse[1]	preventing recurrence[2]

1. Relapse: the symptoms return and are severe enough to meet the criteria for MDD within 6 months following remission.
2. Recurrence: a new episode of MDD

Guidelines also suggest frequent outpatient follow-up visits in the acute phase in order to provide patient support, adjust dosage, and monitor side effects and clinical response. The AHCPR panel recommends that patients be seen every 10 to 14 days for the first 6 to 8 weeks or more frequently with more severe depression.[8] The APA also recommends that patients be seen on a weekly basis during the acute phase.[9] There is no current recommendations on appropriate interval of visits specifically for continuation phase, but AHCPR panel suggests that visits every 4 to 12 weeks are reasonable once the depression has resolved.

1.2.5 Quality of Antidepressant Treatment in Practice

Routine management for depression still falls short of guideline recommendations. Only half to two thirds of patients with confirmed MDD receive any health care.[1, 10] Among those seeking healthcare, only one fourth received appropriate treatment.[1, 11] The National Committee on Quality Assurance (NCQA) assesses quality of care of healthcare organizations every year based on the Healthcare Effectiveness Data and Information Set (HEDIS) antidepressant medication management measures.[36] According to NCQA's 2004 annual report, 11-20% of MDD patients receiving antidepressant treatment had optimal follow-up visits, 46-61% completed acute phase treatment, and 29-44% completed continuation phase treatment.[37] Past empirical studies using similar HEDIS measures found

that 27%-62% of depression patients receiving treatment had optimal follow-up visits[4, 6, 18], 11%-65% completed acute phase treatment[2-7], and 42%-44% completed continuation phase treatment.[2, 6] In general, patients with MDD obtained suboptimal pharmacotherapy management and inconsistent follow-up visits.[38]

1.3 Previous Research

Prior research in this area is reviewed below in two major sections. The first section describes the differences in care patterns between generalists and specialists. The second section summarizes: 1) studies examining the types of providers seen by patients with MDD; 2) studies examining outpatient follow-up visits; 3) studies examining the factors associated with antidepressant treatment patterns; 4) studies investigating the association between provider specialty, antidepressant treatment patterns and healthcare utilization.

1.3.1 Differences between Generalists and Specialists

A body of literature comparing care patterns between generalists and specialists is accumulating. Despite the variety of specialty areas, the findings generally suggest that specialists are more knowledgeable about their area of expertise;[39-41] they are more likely to use novel medications and technology;[39, 41] they are more likely to comply with guidelines;[41] and they are more likely to use more resources.[40, 41] Specialists, with advanced education and training, typically have a superior knowledge about specific clinical conditions than generalists. Specialists treat a narrower range of clinical problems, so they can focus on updating the technology and continuing education related to their therapeutic area. With greater exposure to the latest medical information in a particular therapeutic area, specialists adopt emerging technologies more aggressively than generalists. Specialists may have greater exposure of the guidelines via specialty training or professional activities, and the number of guidelines is typically smaller than general medicine. Specialists are qualified to perform many diagnostic and therapeutic procedures which may increase costs of care.

The majority of studies comparing generalists to specialists have typically been based on observational study designs, which are subject to selection and patient case-mix

differences.[39, 42] Studies favoring specialists were less likely to adequately address case-mix adjustment.[42] In addition, many studies failed to address the characteristics of the physicians such as physician gender, years of practice, and patient volume.[42] In this dissertation, we attempt to improve upon prior studies comparing depression care between primary care providers and psychiatrists by utilizing multivariable analyses with adjustment of comorbidities with application of propensity score matching.

1.3.2 Literature Relevant to Specific Aims

1.3.2.1 Aim 1: Types of Providers Seen by Patients with MDD

Research Aim 1 examines the patient characteristics in the choice of provider specialty to initiate antidepressant therapy for treatment of MDD. Three major sources have been used to identify provider specialty type in prior studies that examined depression care by provider specialty: 1) type of clinic or location of the initial visits, 2) type of provider seen during a visit, and 3) type of provider who wrote a prescription for an antidepressant. The following section describes each source in detail and reports their findings (Table 1.3).

Table 1.3 Summary of Studies Examining Provider Specialty

Study	Study population	Sample size	Data used to define provider specialty	Care categories	Significant differences in patient characteristics
Akincigil, 2007[2]	Commercially insured 2003-2005	4,312	Type of provider on initial visit	Mental health professional; general medical care	None examined
Bambauer, 2007[13]	Commercially insured 2002-2004	11,878	Initial prescribing provider from prescription drug claims	Primary care physician (PCP), psychiatrist, physician with other specialty	Age, gender, comorbidities, multiple prescribing provider, use of multiple antidepressant, antidepressant type
Busch, 2004[43]	VA 2000-2001	27,713	Type of clinic of initial visit	MD in mental health clinic, MD in non-mental health clinic, non-MD in mental health clinic, non-MD in non-mental health clinic, missing	None examined
Charbonneau, 2003[3]	VA 1999	12,678	Type of clinic of initial visit	Primary care clinic only, primary care clinic and psychiatry clinic, psychiatry clinic only, and other clinical settings only.	None examined
Fairman, 1998[15]	Commercially insured 1994-1995	3,101	Initial prescribing provider from prescription drug claims	Non-specialist, psychiatrist, non-psychiatric specialist	Age, gender, insurance type, previous totally monthly drug cost, chronic disease score
Hylan, 1999[16]	Commercially insured 1993-1994	1,034	Provider specialty of initial outpatient visit	Family practitioner, other non-specialist health care clinicians, acute care clinic or other primary care setting, and psychiatrist	None examined
Jones, 2006[4]	VA 1997-2005	2,178	Type of clinic of initial visit	Inpatient, primary care, mental health and other outpatient	None examined
Robinson, 2006[6]	Commercially insured 2001-2004	60,386	Billed contact coded with a psychiatrist, mental health and chemical dependency treatment facility, psychologist, or psychiatric nurse	Received any mental health specialty care or not	None examined
Simon, 2001[7]	Commercially insured 1994-1996	369	Prescribing provider from prescription drug claims	PCP and psychiatrists	Age, gender, emotional role, social function, physical function, physical role, prior specialty care
Weilburg, 2003[17]	Commercially insured 1996-1999	1,550	Prescribing provider from prescription drug claims	PCP only , psychiatrists only, and other provider type only, PCP and psychiatrist, PCP and other, psychiatrist and other, PCP and psychiatrist and other	None examined

Type of clinic or location of the initial visit

Three Veterans Administration (VA) studies used type of clinic or location code from service claims of the outpatient visits to identify provider type because specific provider codes were unavailable. Jones et al. used location of initial depression diagnosis (inpatient, primary care, mental health and other outpatient) as the definition of provider specialty.[4] They found that majority of their study population received care in a primary care outpatient clinic (65%), while 21.4% of patients were diagnosed in a mental health outpatient clinic. Busch et al. also used initial clinic type but with a more detailed categorization.[43] They found 49% of subjects were diagnosed by a medical doctor (MD) in a mental health clinic, 12% by a MD in a non-mental health clinic, 3% by a non-MD in a mental health clinic, and 6% by a non-MD in a non-mental health clinic. The provider variable was missing in 31% of subjects. Charbonneau and colleagues[3] classified the type of clinic where care was provided during a three month profiling period into 4 categories: primary care clinic only, primary care clinic and psychiatry clinic, psychiatry clinic only, and other clinical settings only. They found 26% of patients went to a primary care clinic, 21% of patients went to a psychiatry clinic, and 40% of patients went to both. None of these studies examined patient differences by provider specialty

Location of diagnosis visit does not necessarily identify the type of provider a patient has seen because primary care clinics might receive collaborative support from psychiatrists during the visits. Therefore, this source might not truly identify the type of provider that truly managed patients' antidepressant treatment.

Type of provider seen during a visit

Three studies utilized provider specialty codes from service claims of outpatient visits to identify provider specialty. Robinson and colleagues used a dichotomous variable to indicate whether the patient received any mental health specialty care. [6] If patients had any billed contact coded with a psychiatrist, mental health and chemical dependency treatment facility, psychologist, or psychiatric nurse during the study period, they were characterized as receiving mental health specialty care which accounted for 13.8% of their study population. Hylan and colleagues[16] categorized initial provider into family practitioner, other non-specialist health care clinicians, acute care clinic or other primary care setting, and psychiatrist. They found 32% of patients had seen family practitioner as their initial provider, 8% had seen a non-specialist health care clinician as their initial provider, 27% had been treated in other acute care clinic or other primary care setting, and 33% had seen a psychiatrist as their initial provider. Akincigail and colleagues went a step further to examine types of provider on initial visit and follow-up separately.[2] Among the study population, 50.5% of patients saw a general medical provider in an initial visit and 49.5% saw a mental health professional. They did find that 27.7% of patients had follow-up with a psychiatrist and 23.7% of patients with other mental health providers. None of these studies compared patient characteristics by provider specialty. The provider identified from outpatient visits may not accurately reflect the provider that managed antidepressant treatment if patients see different providers to obtain antidepressant prescriptions.

Type of provider who wrote a prescription for an antidepressant

Four studies identified provider based on provider specialty identified from prescription claims. Simon et al. dichotomized their patients as treated by primary care providers and psychiatrists.[7] In their study, 55% of patients were initially treated by a

primary care provider, and 45% by a psychiatrist. They found that patients treated by psychiatrists were younger, more likely to be male, and more impaired in emotional role and social function. Fairman and colleagues categorized initial prescriber into non-specialist, psychiatrist, and non-psychiatric specialist.[15] They found 41% of initial antidepressant prescriptions were written by non-specialists, 32% by non-psychiatrist specialists, and 13% by psychiatrists. They found patients initially prescribed an antidepressant by a psychiatrist were more likely to be younger, male, in an indemnity plan, have lower chronic disease score, and have lower previous monthly drug costs.[15]

Bambauer and colleague defined initial prescriber into three categories: primary care physician, psychiatrist, and physician with other specialty.[13] In their study population, 67% of patient's antidepressant was initially prescribed by a primary care physician, 20% by a psychiatrist, and 13% by a non-psychiatric specialist. They found that patients treated by psychiatrists were more likely to be younger and male than patients treated by other physicians. Patients whose treatment was initiated by a non-psychiatric specialist were more likely to see more than one type of provider during the treatment episode, while patients treated by psychiatrists were more likely than other patients to use more than one type of antidepressant during the treatment episode.

Weilburg and colleagues[17] looked at more detailed provider combinations beyond the initial prescriber. Prescribing providers were assigned into three categories: primary care physicians, psychiatric specialists, and non-psychiatric specialists, resulting in seven different combinations of providers (Table 1.3). They found more patients with prescriptions written solely by psychiatric specialists (28%) than solely by primary care physicians (26%) or

solely from other provider types (18%). 28% of patients had prescriptions written by multiple types of providers. They did not examine patient differences by provider specialty.

Several sources have been utilized to identify provider type. Only three studies examined the baseline characteristics between patients receiving care from different provider specialties.[7, 13, 15] To isolate the provider effect, one must consider patient case-mix between generalists and specialists. The Medical Outcome Study (MOS) is an observational study of the differences in process and outcomes of care of patients from a wide range of plans.[44] Particularly, patients were screened with a depression case finding procedure which allows further analysis for differences of depressed patients receiving care from various payment settings and provider specialties.[45] Among characteristics of depressed patients, sickness has the strongest effect on the probability of specialty care.[46] Mental health specialists, especially psychiatrists, encountered more severely depressed patients.[47] Patients of mental health specialists tend to have worse mental health and more limitations in social activities compared with patients of medical clinicians. On the other hand, patients of medical clinicians had worse physical functioning and worse health perceptions.[48]

Most of the studies listed in Table 1.3 failed to examine patient differences among provider specialties. This dissertation extends the earlier work by identifying the provider specialty based on index antidepressant which we considered as a more reliable source of provider specialty because specialty information based on clinic or visit may not correctly identify the types of providers who managed antidepressant treatment if the visits provider did not prescribe an antidepressant or the clinic received collaborative support from different types of providers. In the present study, patient characteristics were examined by the following three distinct groups who received index antidepressant from: 1) a primary care

provider; 2) a psychiatrist; 3) a non-psychiatric specialist, which is comparable to the definitions used by Bambauer et al.[13]

1.3.2.2 Aim 2: Outpatient Follow-up Visits

This aim seeks to understand whether receipt of guideline-concordant outpatient follow-up visits during acute phase varies by initial prescriber specialty among patients with MDD treated with antidepressant. Five studies have examined the frequency of outpatient follow-up visits, and three included provider specialty as a predictor in their analysis (Table 1.4). [4, 6, 7]

Table 1.4 Summary of Studies for Completion of Outpatient Follow-up visits

Study	Study population	Sample size	Definition of adequate follow-up care	Percentage population achieving adequate follow-up care	Significant predictors of adequate follow-up visits
Charbonneau, 2003[3]	VA 1999	12,678	at least 3 visits with a CPT code for psychotherapy/medication management, ICD-9 code for depression, or visits made to primary care or psychiatry clinics within 3 months of the initial depression encounter	62%	Not measured
Jones, 2006[4]	VA 1997-2005	2,178	at least 3 visits to primary care or psychiatry clinics within 3 months of the initial depression encounter	27%	Increased medical and psychiatric comorbidity, and diagnosis in a non-primary care clinic
Morrato, 2008[49]	Commercially insured 1998-2005	193,151	At least 3 billable claims for contacts with a primary care or mental health practitioner coded with a mental health diagnosis during the 84 days following the new diagnosis and at least one of the three follow-up contacts must be with a prescribing practitioner (HEDIS)	40%	Not measured
Robinson, 2006[6]	Commercially insured 2001-2004	60,386	HEDIS	44%	Comorbid anxiety, comorbid bipolar, non-capitated insurance, any mental health specialty care, age
Simon, 2001[7]	Commercially insured 1994-1996	369	HEDIS	57% for patient treated by psychiatrists and 26% by PCP	Initially treated by psychiatrists

Jones et al. and Charbonneau et al. investigated follow-up care for depression in a VA population based on the VA depression guidelines that define adequate follow-up care as at least 3 visits to primary care or psychiatry clinics within 3 months of the initial depression encounter.[3, 4] Charbonneau and colleagues found that 62% of veterans received guideline-concordant follow-up visits, but they did not assess whether receipt of guideline-concordant follow-up visits differ between patients initially treated in primary care and in mental health clinics. Jones and colleagues found that 27% of subjects received three or more visits within 12 weeks and initial diagnosis in a mental health clinic was the most significant predictor of adequate follow-up care (OR=4.15, 95% CI: 2.86-6.01).[4]

Robinson et al. used a definition of optimal practitioner contacts from the NCQA HEDIS measures[6] which define optimal follow-up as at least 3 billable claims for contacts with a primary care or mental health practitioner coded with a mental health diagnosis during the 84 days following the new diagnosis and at least one of the three follow-up contacts must be with a prescribing practitioner, the same definition used in this dissertation. They found that 44.3% of depressed patients in commercially insured population had adequate follow-up care. Receipt of mental health specialty care was the most significant predictor of adequate follow-up care (OR=5.83, 95% CI: 5.62-6.06). Using the same HEDIS measure, Morrato et al. found that 40% of patient had adequate follow-up care.[49] Simon et al. found that a significantly higher proportion of patients treated initially by psychiatrists had adequate follow-up care than patients treated initially by primary care (57% vs. 26%, $p<0.01$). [7]

Despite the difference in definitions, these five studies showed that the follow-up care for antidepressant users is suboptimal, but initial treatment by a mental health provider or in a mental health clinic was the most important factor associated with adequate follow-up care.

1.3.2.3 Aim 2: Antidepressant Treatment Patterns

In recent years, ten studies have examined refill adherence patterns among antidepressant users. The following section describes the studies that include either mental health specialty care or follow-up visits as covariates in predicting antidepressant adherence (Table 1.5).

Table 1.5 Summary of Studies Examining Predictors of Antidepressant Adherence

Study	Study population	Sample size	Antidepressant use measure	Identification of mental health specialty care	Identification of optimal follow-up visits	Other significant predictors of antidepressant adherence
Akincigil, 2007[2]	Commercially insured 2003-2005	4,312	Acute phase adherent: MPR>=75% during first 16 weeks after treatment initiation. Continuation phase adherent: MPR>=75% during week 17-33	Y (significant)	N	Older age, higher income, no headache or migraine, no CVD/diabetes, more number of medications excluding psychotropics, newer-generation antidepressant, no other substance abuse
Bambauer, 2007[13]	Commercially insured 2002-2004	11,878	Whether patients filled their index antidepressant prescription (immediate non-adherence)	Y (significant)	N	Initial antidepressant type
			Less than 52 days without antidepressant treatment during the 180-day episode of treatment was considered adherence	Y (not significant)	N	Older age, no prior use of pain medication, treatment by multiple providers, antidepressant type.
Busch, 2004[43]	VA 2000-2001	27,713	At least 84 days (acute treatment phase), and 180 days (continuation phase) during a 180 days follow up period	Y (not significant)	N	Older age, women, married patients, higher income, comorbid mental health diagnosis
Charbonneau, 2003[3]	VA 1999	12,678	Refill adherence with MPR >79% during a fixed 3-month calendar profiling period (June 1, 1999 to August 31, 1999) was deemed adequate. The patient could be in acute, continuation, or maintenance phases.	Y (significant)	N	White race, married
Fairman, 1998[15]	Commercially insured 1994-1995	3,101	Termination of antidepressant treatment before or on first month	Y (not significant)	N	Older age, female, newer-generation antidepressant
Hylan, 1999[16]	Commercially insured 1993-1994	1,034	Dichotomous. 1=had four or more prescriptions without switching or augmentation	Y (significant)	N	Female, present of other mental diseases
Jones, 2006[4]	VA1997-2005	2,178	Refill adherence with MPR>=80% in 12 weeks was deemed adequate	Y (not significant)	Y (significant)	Female, not married, higher number of medical or psychiatric comorbidities
Robinson, 2006[6]	Commercially insured 2001-2004	60,386	Effective acute-phase treatment: at least 84 days of supply of antidepressant during the first 114 days. Effective continuation-phase treatment: at least 180 days of supply of antidepressant during the first 214 days.	Y (significant)	N	Newer-generation antidepressant, older age, female, higher wage, less medical comorbidity, capitated insurance
Simon, 2001[7]	Commercially insured 1994-1996	369	Received at least 90 days of continuous antidepressant treatment at a minimally adequate dose	Y (not significant)	N	-
Weilburg, 2003[17]	Commercially insured 1996-1999	1,550	Treatment adequacy was defined with at least one trial of an average daily dosage of 20mg fluoxetine equivalents of a period of 90 days	Y (significant)	N	Newer-generation antidepressant

Ten studies examined adherence patterns in four ways: 1) early termination, 2) prescription refill count during follow-up period, 3) adherence during a fixed calendar profiling period, and 4) adherence during guideline-concordant acute and continuation phases.

Early termination

In a commercially insured population, Fairman et al.[15] defined early termination of antidepressant if the length of therapy was less than 30 days. Receipt of an initial antidepressant prescription from a non-psychiatrist was associated with a 28% increase in the odds of one-month termination compared to receipt from a psychiatrist, even though it was marginally statistically significant (p=0.052).[15] Bambauer and colleagues examined factors predicting whether patients ever filled their index antidepressant prescription (immediate non-adherence).[13] They found that being treated by a psychiatrist was associated with significantly lower odds of immediate non-adherence (OR=0.7, 95%CI: 0.61-0.8), while being treated by physician with other specialty was associated with significantly higher odds (OR=1.39, 95%CI: 1.22-1.6) compared with patients treated by primary care physicians.

Prescription refill count during follow-up period

Hylan et al. found that the odds of receiving four or more antidepressant prescription refills in six months after initial diagnosis were significantly lower for patient initially seen during an office visit by a family practitioner, in other non-specialist healthcare clinic, and other acute care clinic compared with patient initially seen by a psychiatrist.[16] Their measure did not consider the actual days-of-supply with each refill record, and count of number of refills might not be able to precisely capture the actual consumption of antidepressant. A more stringent measure with consideration of days-of-supply and intervals between refills is necessary to more correctly measure the antidepressant adherence.

Adherence during a fixed calendar profiling period

In a VA sample, Charbonneau et al. defined duration adequacy as antidepressant refill adherence with medication possession ratio (MPR) >75% during a fixed 3-month calendar profiling period (June 1, 1999 to August 31, 1999). Because the antidepressant treatment period was cross-sectional, the profiling period could have been in acute, continuation, or maintenance phases of the treatment depending on a patient's index diagnosis date. They found that receipt of care exclusively from a primary care clinic significantly reduced the probability of adequate antidepressant duration (OR=0.84, 95% CI: 0.72-0.94).[3]

Adherence during guideline-concordant acute/continuation phases

Three studies investigated adherence with a guideline-concordant acute phase[4, 7, 17], and four studies examined both acute and continuation phases.[2, 6, 13, 43] In a VA sample, Jones et al. defined antidepressant duration adequacy in acute phase if refill adherence had an MPR greater or equal to 80% in the first 12 weeks.[4] They found that adequate outpatient follow-up (three or more during acute phase) was associated with increased odds for duration adequacy of acute phase antidepressant therapy (OR=2.1, 95% CI: 1.54-2.88), but initial diagnosis from mental health clinic was non-significant. This study included both optimal follow-up and location of initial diagnosis as covariates in the model predicting duration adequacy in acute phase. Simon and colleagues found that the proportion of patients receiving 90 days of continuous antidepressant therapy at minimally adequate dose was similar between primary care patients and patients initially treated by psychiatrists and patients initially treated by primary care providers.[7] Weilburg et al. defined treatment adequacy as at least one trial of an average daily dosage of 20mg fluoxetine equivalents of a period of 90 days.[17] Compared with patients receiving antidepressant prescriptions from primary care providers exclusively, they

found that the patients being cared by the following combination of providers were more likely to have adequate antidepressant treatment: primary care and other types of providers (OR=2.33, 95% CI: 1.56-3.48), psychiatrist exclusively (OR=2.64, 95% CI: 1.97-3.55), primary care and psychiatrist (OR=3.29, 95% CI: 1.99-5.51), psychiatrist and other type of providers (OR=5.04, 95% CI: 3.29-7.81), and primary care, psychiatrist, and other type of providers (OR=5.13, 95% CI: 2.86-9.61).

Busch et al., Bambauer et al., Akincigil et al, and. Robinson et al. conducted retrospective studies using HEDIS measures to define adherence in acute and continuation phases, which are most closely concordant with guideline recommendations.[2, 6, 13, 43] Busch et al. examined whether veterans remained on antidepressant treatment for at least 84 days (acute treatment phase) and 180 days (continuation phase).[43] They found that antidepressant adherence did not differ between patients treated in a mental health clinic and patients treated in a non-mental health clinic. Bambauer et al defined adherence as having less than 52 days without antidepressant treatment during the 180-day episode of treatment.[13] They found that being initially prescribed by physicians with other specialty was associated with an increased risk of non-adherence (OR=1.4, 95% CI: 1.24-1.59) compared with patients treated by primary care physicians, but no differences were found between primary care physicians and psychiatrists. In addition, treatment by multiple providers was associated with lower odds of non-adherence (OR=0.83, 95% CI: 0.75-0.92). Akincigil et al. defined acute phase adherence as refill adherence with an MPR $\geq$ 75% during first 16 weeks after treatment initiation.[2] Among patients who were adherent in acute phase, continuation phase adherence was defined as refill adherence with an MPR $\geq$ 75% from 17th to 33rd week. They found that initial provider type was not significant in predicting adherence, but follow-up with a

psychiatrist was associated with higher odds of adherence in both the acute (OR=1.19, 95% CI: 1.03-1.38) and continuation phases (OR= 1.25, 95% CI: 1.02-1.53). Robinson et al. defined effective acute phase treatment as at least 84 days-of-supply of antidepressant during the first 114 days following initiation of the index antidepressant, and effective continuation phase treatment as at least 180 days-of-supply of antidepressant during the first 214 days following initiation of the index medication.[6] They found that receipt of any mental health specialty care by a psychiatrist, mental health and chemical dependency treatment facility, psychologist, or psychiatric nurse significantly increased the odds of adherence in both the acute (OR=1.38, 95% CI: 1.33-1.43) and continuation phases (OR=1.46, 95% CI: 1.41-1.51).

In summary, five out of ten studies showed that patients with some form of contact with mental health specialists had better antidepressant adherence (Table 1.5). Several approaches have been used to evaluate antidepressant adherence. Studies using early termination might preclude inference beyond treatment initiation and measure based on prescription count is less precise without considering the days-of supply of each refill as well as the intervals between refills. Use of antidepressants can be more precisely estimated if the patients are followed when they initiate antidepressant treatment. The definition of provider specialty varied widely across prior studies. As discussed in 1.3.2.1, this dissertation used provider specialty based on index antidepressant as the source of information which gives a closer link to the actual provider who prescribed, and most likely, managed a patient's antidepressant therapy. In addition, only one study included both mental health specialty care and follow-up visits as covariates in the regression model predicting antidepressant adherence in a VA sample.[4] This dissertation contributes to the literature by measuring

provider effect with control over receipt of guideline-concordant outpatient follow-up visits during acute phase in a non-VA sample.

1.3.2.4 Aim 3: Provider Specialty, Antidepressant Treatment and Healthcare Utilization

Aim 3 of this dissertation examined whether provider specialty and completion of antidepressant treatment are associated with differences in subsequent healthcare utilization. The next section describes the prior research in this area.

Prior literature suggests that specialists tend to use more resources than generalists.[40, 41] Literature specifically examining differences for provider specialty in utilization for mental health illness is scarce. It was found that patients treated in the mental health specialty sector had higher expenditures and hypothesized that it was due to a combination of longer episodes and more intensive treatment. [6, 50, 51] Only one study conducted by Sewitch et al. based on a Canadian population used all-cause hospitalization as an outcome and they found that being diagnosed by a psychiatrist significantly increased the odds of hospitalization (OR=2.76, 95% CI=1.62-4.68)[19] (Table 1.6). This dissertation adds to the literature by examining this association in the U.S. population.

Table 1.6 Summary of Studies Examining Provider Specialty, Antidepressant Treatment Patterns and Future Healthcare Utilization

Study	Study population	Sample size	Main healthcare utilization outcome	Provider Specialty	Antidepressant use measure	Major findings	Other predictors of healthcare utilization
Charbonneau, 2004[18]	VA 1999	12,678	All-cause and psychiatric hospitalization	None	Refill adherence with MPR >79% during a fixed 3-month calendar profiling period (June 1, 1999 to August 31, 1999) was deemed adequate	Adequate duration of antidepressant therapy significantly reduced the risk of psychiatric hospitalization, but it was marginally significant in risk of all-cause hospitalization (p=0.05)	All-cause hospitalization: older age, black race, prior hospitalization, higher comorbidity index, alcoholism Psychiatric hospitalization: younger age, male, black race, not married, prior hospitalization, lower comorbidity index, alcoholism, PTSD
Sheffield, 2003[20]	Commercially insured 1996-1997	566	Depression-related hospitalization	None	1) switching and augmentation if received another antidepressant in place of or in addition to the index drug during 12-month period, 2) discontinuation if patients had less than 120 days of continuous index therapy, 3) stable if had at least 120 days of continuous index therapy	Switching/augmentation was associated with increased risk of depression-related hospitalization compare to stable group. No difference was found between discontinuation and stable group.	prior outpatient visits
Sewitch, 2007[19]	Canadian public insured 2000-2001	2,047	All-cause emergency room visits and all-cause hospitalization	Initial diagnosis by primary care provider or psychiatrists	Minimum supply of 150 days' worth medication in a 180 days period	Adequate duration of antidepressant treatment was not associated with risk of emergency room visits or hospitalization. Initial diagnosis by psychiatrists increased the likelihood of all-cause hospitalization	ER: male, personality disorder, substance dependence, insurance type hospitalization: age, comorbidity, personality disorder, substance dependence

There are three studies identified that examined the association between antidepressant treatment and subsequent hospitalization and/or emergency room visits (Table 1.6). Sheffield and colleagues examined how differences in antidepressant usage patterns affect the risk of depression-related hospitalization among persons taking three selective serotonin reuptake inhibitors (SSRI) for their depression.[20] They categorized the usage patterns into three groups: switch/augmentation, discontinuation, and stable. They found that patients whose therapy was switched or augmented were 3.17 (95% CI: 1.26-7.99) times more likely to require hospitalization related to their depression than those patients whose therapy was stable. Their study was limited to three SSRI agents, which reduced the generalizability of the results. In a VA sample, Charbonneau and colleagues found that adequate antidepressant duration was associated with lower risk of psychiatric hospitalization (OR=0.82, 95% CI: 0.69-0.96), and the change in risk of all-cause hospitalization was marginally significant (OR=0.9, 95% CI=0.81-1.0).[18] Sewitch et al. found that duration adequacy (150 days-of-supply antidepressants during a 180-days period) was not associated with risk of emergency room visit or hospitalization during 1-year follow up period in a Canadian public insured population.[19]

Charbonneau et al has found a protective effect of adequate use of antidepressant over risk of psychiatric hospitalization among veterans[18], and it is necessary to generalize the results to other population. The dissertation achieves this goal by incorporating guideline-concordant antidepressant treatment patterns measurement with inclusion of wide selection of antidepressant agents in a more generalized population.

1.4 Significance

Untreated or under-treated MDD may lead to a substantial burden to patients, healthcare systems, and society. This dissertation seeks to provide a comprehensive picture of the care that MDD patients received in a managed care setting.

Aim 1 describes the differences among patient initially prescribed an antidepressant by different types of providers. Before examination of how patients taking antidepressants to treat MDD are managed differently between primary care setting and mental health specialty care setting, it is an important first step to understand whether patients are systematically different between these two settings. This knowledge leads us to correctly measure the provider effect related to outcomes in Aim 2 and Aim 3.

Aim 2 investigates whether receipt of guideline-concordant outpatient follow-up visits during acute phase varies by provider specialty. Empirical studies showed that the follow-up care for antidepressant users is still suboptimal in real-world settings, and it is important to understand what factors are associated with receipt of guideline-concordant follow-up visits. Investigation over patient characteristics may help identify the population who may under the risk of less frequent follow-up. This knowledge can aid clinicians to pay more attention when they encounter these vulnerable patients in their practice, and assist policymakers to develop organizational strategies to target the population who might experience poor follow-up. It is also important to identify modifiable factors, such as access to care and burden of out-of-pocket copayment, where the intervention is plausible. In particular, we examined provider differences in this dissertation. Several studies has shown mental health specialty contact increased the likelihood of more frequent follow-up.[4, 6] This dissertation improves upon by identifying provider specialty based on prescription claims.

We consider this source more accurately represent the actual provider specialty since it is the provider who wrote the prescription and is likely to educate and continue to monitor patient's antidepressant treatment. By examination of level of guideline-concordance for managing antidepressant treatment by provider specialty, the findings can support and justify where the quality improvement for depression care is needed.

Aim 2 also examines whether provider specialty and other factors are associated with antidepressant completion. In addition to the aforementioned significance for follow-up visits model which is applicable to antidepressant completion model, this dissertation also attempt to link the association between guideline-concordant follow-up visits and completion of antidepressant treatment phases. Only one study has examined the association between completion of follow-up visits and antidepressant acute phase completion[4], and this relationship has not been examined in a general population. Findings from this aim will provide empirical evidence of the significance of follow-up care by investigating how it quantitatively reinforce patient's adherence to antidepressant treatment. The promotion of follow-up care for depressed patients could have a more solid ground if positive outcome in treatment adherence can be expected. This dissertation improves upon prior studies by controlling for provider specialty and guideline-concordant follow-up visits simultaneously in a general population of commercially insured patients because leaving out one of the variables may result in bias if their effects on antidepressant treatment completion are not independent.

Linking provider specialty, antidepressant treatment patterns to economic outcomes in Aim 3 is critical. Economic outcomes, such as emergency room visits and hospitalization, have not been widely examined for patients with MDD receiving antidepressant treatment.

These events, although rare, takes up large healthcare costs and also implies worse health of the patients. While resources are limited for quality improvement, it is crucial to understand where the cost saving might be in order to allocate the resources efficiently. In particular, if the cost offset effects of antidepressant therapy in concordant to guideline-recommended duration can be found, we will be able to justify the increase in expenditures associated with prolong antidepressant treatment.

1.5 Summary

This dissertation adds to the literature by carefully examining the relationship between provider specialty, guideline-concordant elements of antidepressant treatment (completion of follow-up visits, acute phase, and continuation phase), and subsequent healthcare utilization. The large sample size of privately insured subjects from a large national plan across the United States increases the generalizability of the results to a privately insured population. While antidepressant treatment remains suboptimal in the real world, the findings from this dissertation will provide valuable information by identifying the types of provider whose practice fell short of guideline recommendations. With further understanding of factors associated with guideline-concordant treatment completion and subsequent healthcare utilization, the knowledge gained from this dissertation will provide empirical evidence to support quality improvement and justify resource allocation to improve quality of care for depression.

CHAPTER II

CONCEPTUAL FRAMEWORK

A conceptual framework is needed to provide context for the specific aims. The conceptual framework of the dissertation is based on Andersen's Behavioral Model and the Chronic Care Model (CCM). Andersen's Behavioral Model and the CCM each contain parts of the relationships that this dissertation intends to examine. Therefore, a new conceptual framework is necessary to bring every aspect of the dissertation into a whole picture. Both models contribute to the framework in identifying the relationships among patient, provider, and health system variables.

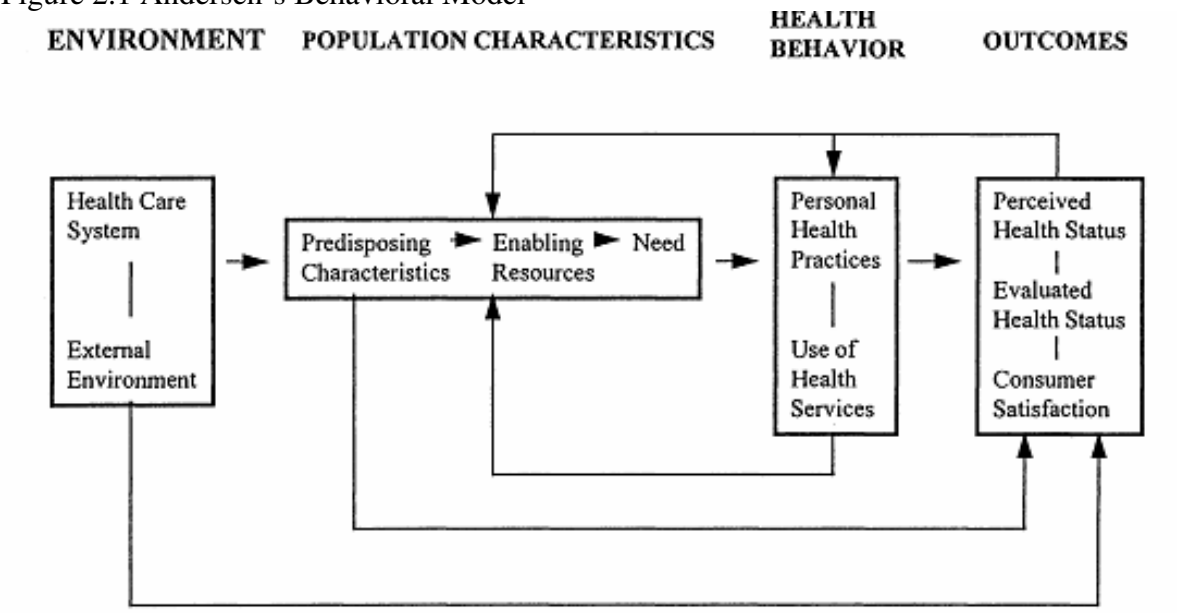
2.1 Theoretical Models

This section describes original theoretical models that were adapted in my conceptual framework.

2.1.1 Andersen's Behavioral Model

Andersen's Behavioral Model (Figure 2.1) was developed in the 1960s to understand why families use health services, and to define, measure, and promote equitable access to healthcare.[52] It was revised in 1995 to incorporate the external environment as an important input for health services and added health outcomes into the model.[53] *Patient* characteristics include predisposing, enabling, and need factors. Predisposing factors include demographic variables (age, gender, and race), socioeconomic variables (education, occupation, and ethnicity), and health beliefs (attitudes, values and knowledge toward health). These variables exist regardless of whether or not a person uses health services. Enabling factor are community resources (health personnel and facilities) and personal resources (income, health insurance) for the use of health services. Enabling factors are considered the most mutable among the three components, and mutability is an important concept in the model because it suggests an opportunity for behavioral change through policies. Need variables include self-perceived needs due to health beliefs, and evaluated needs made by healthcare professionals. They are often the most immediate causes of health service use according to Andersen's Behavioral Model.[53]

Figure 2.1 Andersen's Behavioral Model



Source: Andersen RM. Revisiting the behavioral model and access to medical care: does it matter? J Health Soc Behav 1995;36:1-10

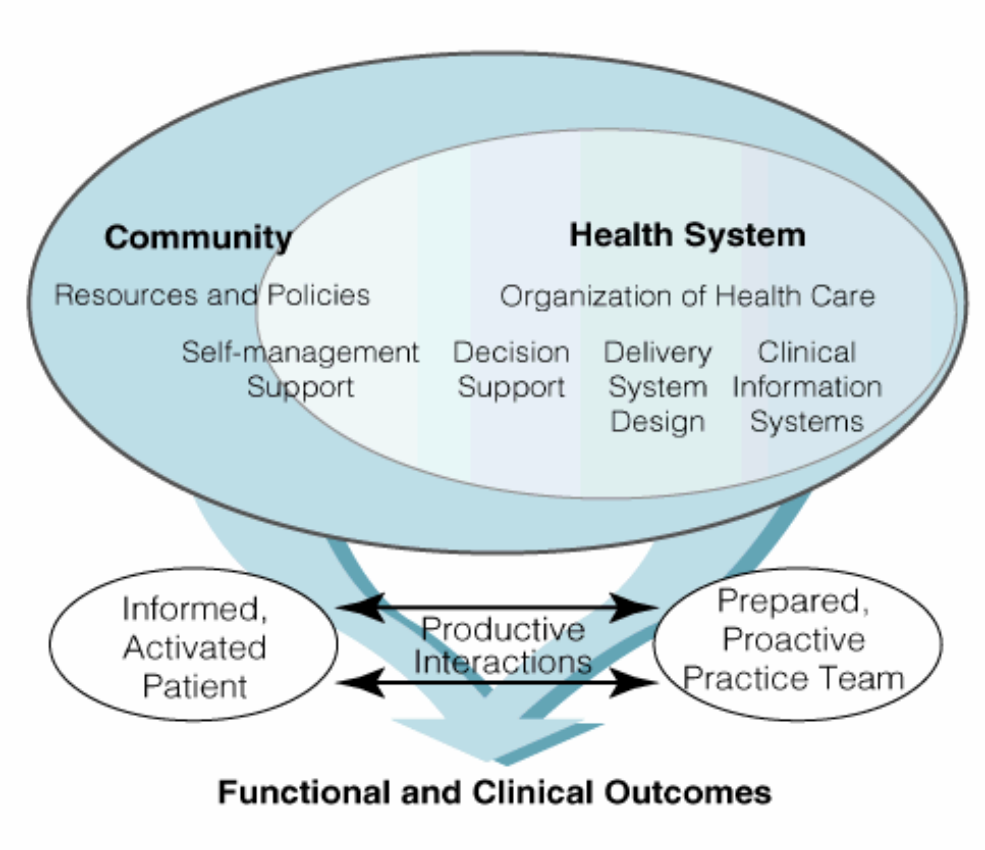
2.1.2 Chronic Care Model

The Chronic Care Model (CCM), developed by Wagner and colleagues during the 1990s, is a model for quality improvement and service redesign.[54] The model emphasizes important interlinked areas of organization to improve care of patients with long term and chronic conditions (Figure 2.2). The elements that involve the community and health system are: self management support, delivery system design, decision support, and clinical information systems. The model highlights the importance of evidenced-based guidelines to inform planned care.[55] The model emphasizes productive interactions between informed patients and prepared providers resulting in improved outcomes.

Medical practices have long been designed to respond to the acute and urgent needs of the patients, particularly in primary care. In the United States, chronic illnesses account for a large portion of healthcare expenditures,[56] but the traditional systems of care do not serve the needs of patients with chronic illness well.[57] The management of healthcare delivery has

undergone substantial reform in recent decades, and systematic reviews have demonstrated that implementing components of the model is associated with significant improved outcomes in patients with chronic diseases such as diabetes mellitus, asthma, depression, and congestive heart failure.[58, 59] In particular, many studies have identified this model as a guide to improve quality of care for treatment of depression.[60, 61]

Figure 2.2 Chronic Care Model

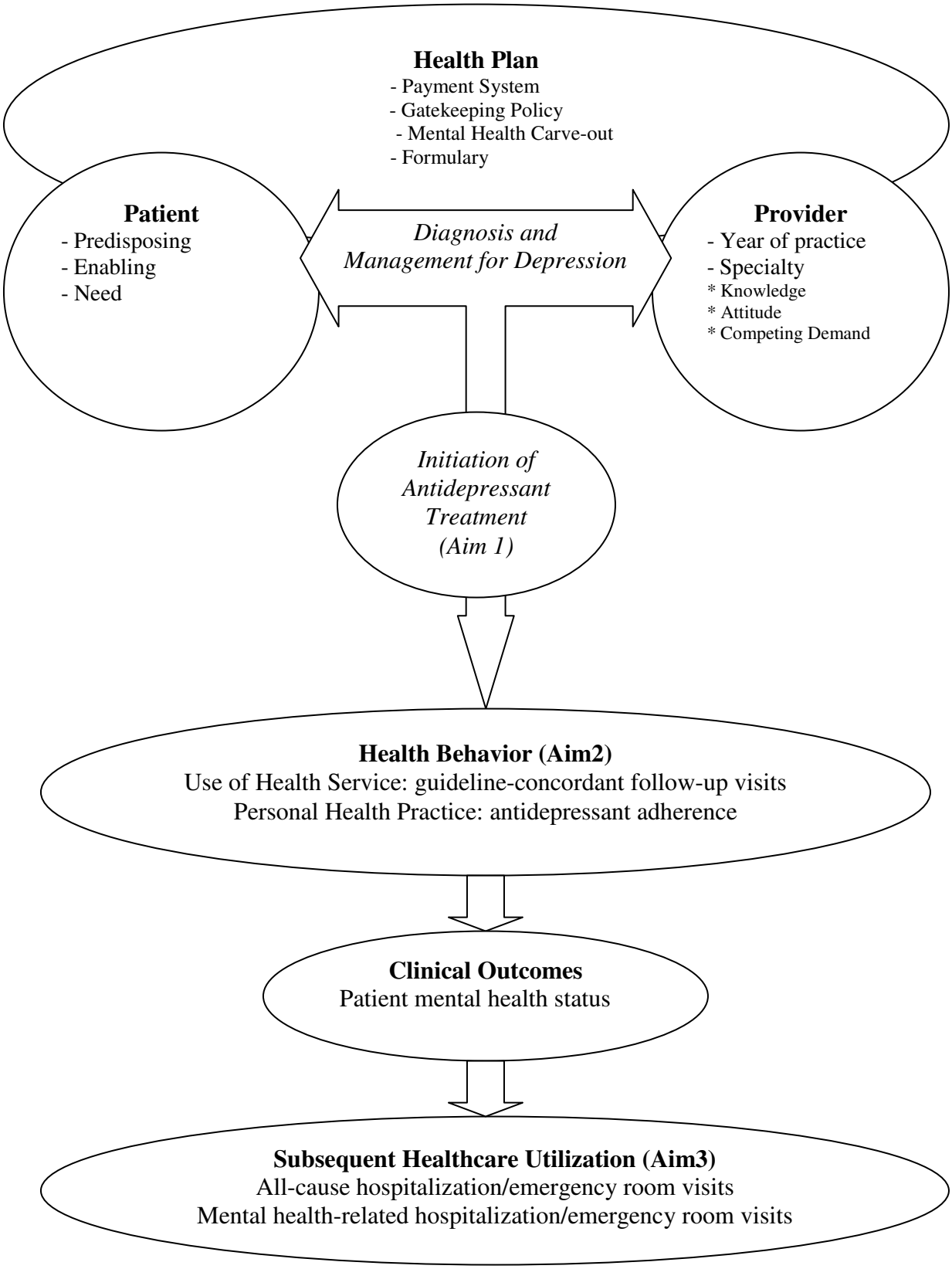


2.2 Conceptual Framework

The conceptual framework for the dissertation, which integrates Andersen's Behavioral Model and the CCM, is presented in Figure 2.3. Andersen's Model provides a framework to link patient characteristics and outcomes of interest, which informs patient *demand* for depression care. In addition, it is crucial to control for patient case-mix and other patient factors to isolate the impact of provider specialty on patient outcomes. The inclusion of patient characteristics can also help identify the population that is vulnerable to poor outcomes.

Even though the purpose of the CCM is to guide practice re-design to improve outcomes among chronically ill patients and this dissertation did not evaluate any intervention for the study population, this model still provides a context for the specific aims examined. The CCM contributes to the conceptual framework by acknowledging the importance of the healthcare system in influencing provider behavior, which informs *supply* differences in provider of depression care. Healthcare systems are the context where the care is *provided*, and healthcare providers are direct personnel to *deliver* the care to patients.

Figure 2.3 Conceptual Framework for the Dissertation



2.2.1 Synthesis of the Conceptual Framework

This section describes the synthesis of the conceptual framework of this dissertation based on the Andersen's Behavioral Model and the CCM in detail (Figure 2.3). The management of depression for these patients occurred under the context of the healthcare system with consideration of characteristics of supply side (provider) and demand side (patient). Once a diagnosis of MDD is made, the decision to initiate antidepressant therapy is determined by patients and providers. This dissertation focuses on the cohort of MDD patients who initiated antidepressant treatment. Patient characteristics were examined among initial prescriber specialties to evaluate confounders for provider effect (Aim 1). It was hypothesized that patients initially prescribed an antidepressant by psychiatrists have greater mental health morbidity, and patients initially prescribed an antidepressant by non-psychiatric specialists have greater physical sickness than patients initially prescribed an antidepressant by primary care providers (PCPs), based on the Andersen's Behavioral Model which suggests need factors are the immediate causes for healthcare utilization.

Patient characteristics are hypothesized to predict follow-up visits, completion of acute and continuation antidepressant phases which are types of health behaviors according to Andersen's Behavioral Model. The CCM suggests that productive interactions could be simulated via community or health system changes derived by evidence-based guidelines, and this concept is relevant to this dissertation that intends to examine guideline components of antidepressant treatment for depression.[55] In this dissertation, it is hypothesized that patients initially prescribed an antidepressant by psychiatrists are more likely to complete follow-up visits, complete acute phase treatment, and complete continuation phase treatment

because psychiatrists are more knowledgeable and to have greater exposure of depression guidelines because of training and practicing environment (Aim 2).

The importance of follow-up has been acknowledged in clinical guidelines by a panel of experts because patients should be carefully monitored in follow-up visits to assess the response of the treatment and the emergence of side effects.[8, 9] Visits should be frequent enough to promote treatment adherence, and to reduce communication gaps between patients and treating physicians about the expected antidepressant therapy duration.[62] Hence, frequent follow-up visits may provide opportunities for patient-provider interactions to reinforce expected duration of antidepressant treatment, aligned to the concepts in CCM. If the communication gap was partially due to patients' failure to remember specific information communicated to them, frequent follow-up could subsequently influence antidepressant adherence. It is hypothesized that patients who received guideline-concordant follow-up visits are more likely to complete antidepressant acute and continuation phase than patients who did not receive guideline-concordant follow-up visits (Aim 2).

Although unobservable, it is assumed that guideline-concordant care will result in better mental health status of the study population and less health care use. According to Andersen's Behavioral Model, patient outcomes can subsequently affect healthcare utilization (Figure 2.1). Patients who complete antidepressant phases are expected to achieve remission or have their depression symptoms under control, which results in better mental health status. This might directly influence the possibility for future health utilization such as mental health-related hospitalization. Uncontrolled depression might also indirectly influence the risk for hospitalization for other medical conditions. Therefore, it is hypothesized that patients with desired antidepressant treatment (defined by completion of phases) as suggested

by guidelines will be less likely to have all-cause hospitalization/emergency room visits and mental health-related hospitalization/emergency room visits compared to those who do not complete (Aim 3).

The direction of provider effect on hospitalization and emergency room is less obvious. Patients treated by psychiatrists might be less likely to suffer from those events due to more guideline-concordant treatment based on the CCM model. If patient characteristics are not perfectly adjusted for in the model, higher risk of those events among patients treated by psychiatrists may partially represent patient effects according to the Andersen's Behavioral Model (Aim 3).

2.2.2 Analytical Model Formulation and Competing Hypothesis

The conceptual framework also guides the dissertation in building the analytical models. It is also important to formulate the possible mechanisms that could explain the variations in outcomes related to provider specialty and identify potential confounding effects.

2.2.2.1 Provider Specialty

This dissertation seeks to understand how provider specialty influences receipt of guideline-concordant follow-up visits, antidepressant treatment phase completion, and subsequent healthcare utilization. The analytical models might only be able to present whether there is any association, but not *why* such difference occurs. It is important to lay out and conceptualize the potential competing hypotheses explaining why provider specialty may impact these outcomes. Several differences between primary care providers and psychiatrists observed in prior literature are *attitudes toward depression*, *knowledge about treatment and guidelines*, and *competing demand*.

Attitudes toward depression. Previous studies have shown that psychiatrists tend to have more favorable attitudes to acknowledge that depression is treatable than PCPs.[63] In addition, it was found that PCPs are less comfortable in dealing with patients with depression and found the work harder and less rewarding than psychiatrists.[64] Such difference in attitudes might influence providers' willingness to continuously treat depression. If attitudes toward depression differ between psychiatrists and PCPs as suggested from the literature, we may expect to see that patients seen by psychiatrists are more likely to receive guideline-concordant follow-up visits and to complete antidepressant treatment compared to those seen by PCPs.

Knowledge about treatment and guidelines. Previous studies have shown that providers with formal qualifications for mental health training were less likely to identify incomplete knowledge about assessment and treatment of depression as a barrier.[65] Being more knowledgeable about efficacy and side effects of antidepressants and more adaptive toward newer agents or approaches may lead to better follow-up care and antidepressant adherence of patients treated by mental health specialists. The CCM also suggests practice based on evidence-based guidelines could simulate productive interactions between patients and providers. Certain barriers for primary care providers to adhere to the treatment guideline are lack of awareness and familiarity.[66] A study showed that only 33.6% of family physicians were aware of the existence of the AHCPR depression guideline one year after its release, and those who were aware were more likely to treat depression and believed they had more knowledge about the treatment.[67] Although we were not able to directly measure the awareness of the guidelines or knowledge toward treatment, we were able to know how

different types of providers perform differently in treating depression by including a guideline-concordant measure of treatment.

Competing demands For most patients, generalists are the first point of contact with the health care system as primary care providers. The Institute of Medicine designates primary care by four major attributes including accessibility, communication, coordination, and comprehensiveness.[68] Hence, generalists usually see more patients and confront a greater variety of illnesses,[69, 70] and face more competing demands for other medical conditions that need to be managed during their visit with patients compared with mental health specialists.[71] This might reduce the time available to educate or communicate with patients about their antidepressant treatment, which may result in poor adherence and reduce the chance for follow-up visits.

In summary, while the higher competing demands that PCPs face is mostly due to the fundamental role as first-line care providers, attitudes toward depression and knowledge about treatment and guidelines are factors more related to difference in training between PCPs and psychiatrists. All the hypotheses listed above lean toward a positive association between psychiatrists and receipt of guideline-concordant follow-up visits and antidepressant treatment completion.

2.2.2.2 Patient Characteristics

In order to correctly model the association of provider specialty, patient characteristics based upon Andersen's Behavioral Model need to be included. Predisposing variables available in the data include age, gender, and region of residence. Some studies found age and gender of patients varied by provider specialties,[13, 15] and several studies found that female gender, and older age of patients were associated with better antidepressant

adherence.[2, 4, 6, 13, 15, 16, 43] However, other predisposing factors which might be predictors in the conceptual framework including race[3], attitudes[72], and stigma[73] are not available.

Examples of need factors observed in the data include comorbidities and other mental health conditions. Evidence from the literature showed that patients seen by psychiatrists had more mental health comorbidities, while patients seen by primary care providers had more of other chronic comorbidities.[13, 15] Poor psychological health increases the probability of obtaining care from a mental-health specialist and poor physical health increases the probability of obtaining care from a general medical provider.[46] Comorbidities may be a burden on adherence because of polypharmacy or stress related to other disease. In addition, comorbidities may compete for the limited healthcare resources that patients have and reduce the possibility to have follow-up visits for depression. Previous studies found that other mental health conditions were associated with antidepressant adherence.[2, 16, 43, 74] In order to accurately estimate the provider effect, case-mix adjustment is crucial. However, depression severity which is the major need factor for our study population is unobservable.

Enabling factors play an important role in determining whether a patient has access to care or medications. The population this dissertation examined is commercially insured, and is homogenous in terms of having health insurance. Unfortunately, there is no information on individual's income or education. Proxies of income and education were created based on individual's state of residence.

Examination of differences in patient characteristics between those who seek care from PCPs and psychiatrists is an important first step in determining how unobservable patient characteristics might confound provider effects. There are several competing hypotheses at

the patient level that arise from Andersen's Behavioral Model. These possible patient factors are: *perceived stigma*, *attitudes toward treatment for depression*, and *depression severity*.

Perceived stigma toward depression. Perceived social barriers may be important obstacles for adherence to pharmacologic treatment, particularly for mental health diseases. In Andersen's Behavioral Model, perceived stigma is a predisposing health belief variable. *Lower perceived stigma* has been found to be associated with better antidepressant adherence.[73] If patients seek different providers based on their perceived stigma, it is likely that PCPs will see patients with more perceived stigma compared with mental health specialists. Receiving care from mental health specialists could be labeled as having mental health issues, so patients with higher perceived stigma might be more reluctant to seek help from them. In such a case, the effect of mental health specialists on patients' antidepressant adherence might be partially explained by differences in patients' perceived stigma. Similarly, patients seen by PCPs might be less likely to make follow-up appointment partially because they are uncertain that depression is a legitimate reason for seeing the doctor due to higher perceived stigma.[75]

Attitudes toward treatment for depression. Attitudes toward depression treatment are also a predisposing health belief variable based on Andersen's Behavioral Model. A study showed that individuals who strongly endorsed specific concerns about antidepressants were reported to have poorer adherence to medication.[76, 77] Compared with mental health specialist patients, the primary care patients had *lower perceived need for care* and *lower levels of acceptability* of evidence-based treatments for depression in a previous study.[72] Patients may be more likely to seek care from the type of provider who will confirm their belief systems and subsequently reject information offered by the physicians that contradict

their beliefs. Such differences may influence whether patients are willing to initiate the treatment as well as whether to continue. Hence, the effect of provider specialty on patients' follow-up visits or antidepressant adherence might be partially explained by patients' own motivation to comply.

Depression severity. Depression severity is a need variable based on Andersen's Behavioral Model. *Higher self-rated severity of illness* has shown to be associated with better adherence to recommended medication regimen among patients with depression.[73] Even though it is reasonable to assume that mental health specialists are more likely to see or be referred more severe or complicated cases, it is unclear whether the ability to adhere will be compromised by self perceived or actual depression severity. If depression severity affects both provider choice and outcomes examined, not being able to control for it will introduce bias of the provider effects.

Among the patient factors that might be relevant to the study analyses, unobserved depression severity is traditionally the concern for secondary data analyses. Furthermore, the direction of its effect on follow-up visits and antidepressant adherence remains unclear. Perceived stigma and attitude toward treatment for depression are hypothesized to confound the provider effect. In other words, the observed effect of receiving care from mental health specialists on follow-up visits and antidepressant adherence in the literature may be due to patients' self-selection. However, perceived stigma, attitude toward treatment for depression and depression severity are unobserved in our data.

2.2.2.3 Health Plan Characteristics

Health insurance plan types and insurance policies may influence access to specialty care medications. Based on the CCM, changes at the organizational level may also have

impact on patient-provider interactions. In the Medical Outcomes Study, it was found that depressed patients in pre-paid plans are significantly less like to see a psychiatrist than patients in fee-for-service plans, and the average patient-provider relationship is significantly shorter in pre-paid plans.[46] Our data do not have individual insurance plan designs such as Preferred Provider Organization or Health Maintenance Organization (HMO). The latter plan usually requires gate-keeping to limit access to specialty care. We could only aggregate claims level data to create some indicators of health insurance plan characteristics. In our model, we included a proxy for initial provider reimbursed on a capitated basis. Reimbursement based on capitation may influence provider's incentive to schedule follow-up. We also do not have information on individual benefit structure such as premium, co-insurance, and copayment. In this dissertation, we used the out-of-pocket copayment recorded on the service claims for primary care provider visits and initial antidepressant prescription drug copayment to as proxies for burden to care.

2.2.2.4 Antidepressant Characteristics

Second-generation antidepressants examined in this dissertation have similar efficacy in the treatment for MDD [78], but individuals may still experience differences in side effects or adverse events. Initial antidepressants were included in the statistical models to control for this aspect. Complex regimen could also impose burden for patients to adhere to antidepressants.[79] Number of pills for daily doses was controlled for such difference between antidepressants.

2.3 Summary

Andersen's Behavioral Model incorporates the outcomes of interests and identifies the *patient* factors that impact the outcomes examined in this dissertation. Controlling for these patient-level potential confounders or modifiers is crucial in isolating the true provider effects. The CCM provides a context of management for depression where characteristics of *healthcare system* and *provider* are supply side factors that explain variation in outcomes.

Laying out the differences in patient and provider characteristics from previous literature also helps understand the potential direction of biases due to unobservable variables, which is important to interpret the results of this dissertation. In addition, outlining the potential reasons for outcomes variation will support interpretation of results and serve as a bridge that leads to future research.

CHAPTER III

METHODS

This chapter discusses the data and the sample selection for the dissertation (Section 3.1). Variables are described (Section 3.2) and statistical models and power analyses for each aim are presented (Section 3.3, 3.4). Sensitivity analysis (Section 3.5), statistical issues (Section 3.6), and limitations (Section 3.7) are discussed.

3.1 Data Source

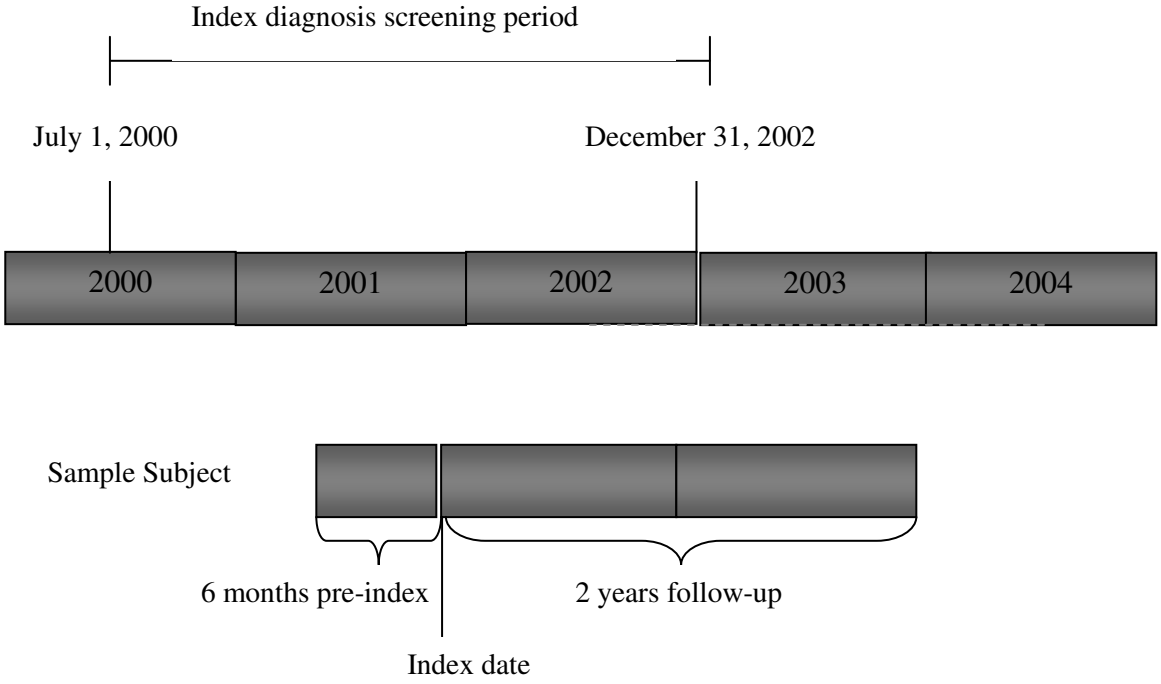
The data for this study originated from a large national health plan affiliated with i3 Innovus with working-age adults and their dependents. The underlying population is geographically diverse across the United States. The data are from January 1, 2000 to December 31, 2004, and organized as four files: member enrollment, service claims, facility claims, and prescription claims. Files can be linked by encrypted patient identifier. Details of variables included in each file are listed in Appendix 2.

3.2 Study Design and Sample

This study was conducted using a retrospective cohort design. The advantages of a retrospective cohort study include being much less costly than other types of study designs (e.g. randomized controlled trial), enabling large sample sizes, and no need to wait for outcomes to occur like prospective cohort studies. Because retrospective cohort studies rely on existing records, some information might be unavailable or otherwise un-collectible.[80] In addition, causal inference depends on strength of design.

To be included in this sample, patients had to meet the following inclusion criteria: 1) they were diagnosed with major depressive disorder (MDD) single episode between July 1, 2000 and December 31, 2002 using the ICD-9-CM (the International Classification of Diseases, 9th revision, Clinical Modification) diagnosis code of 296.20-296.24 in any diagnosis field; 2) they had to have been continuously enrolled for at least 6 months prior to index diagnosis to control for pre-diagnosis characteristics; 3) they had to have been continuously enrolled for at least 2 years after index diagnosis so there was enough follow-up time to observe the outcomes of interests; and 4) they filled a second-generation antidepressant prescription claim within 45 days of the index diagnosis. The timeframe for the cohort and the pre-period and follow-up for a typical subject are listed in Figure 3.1.

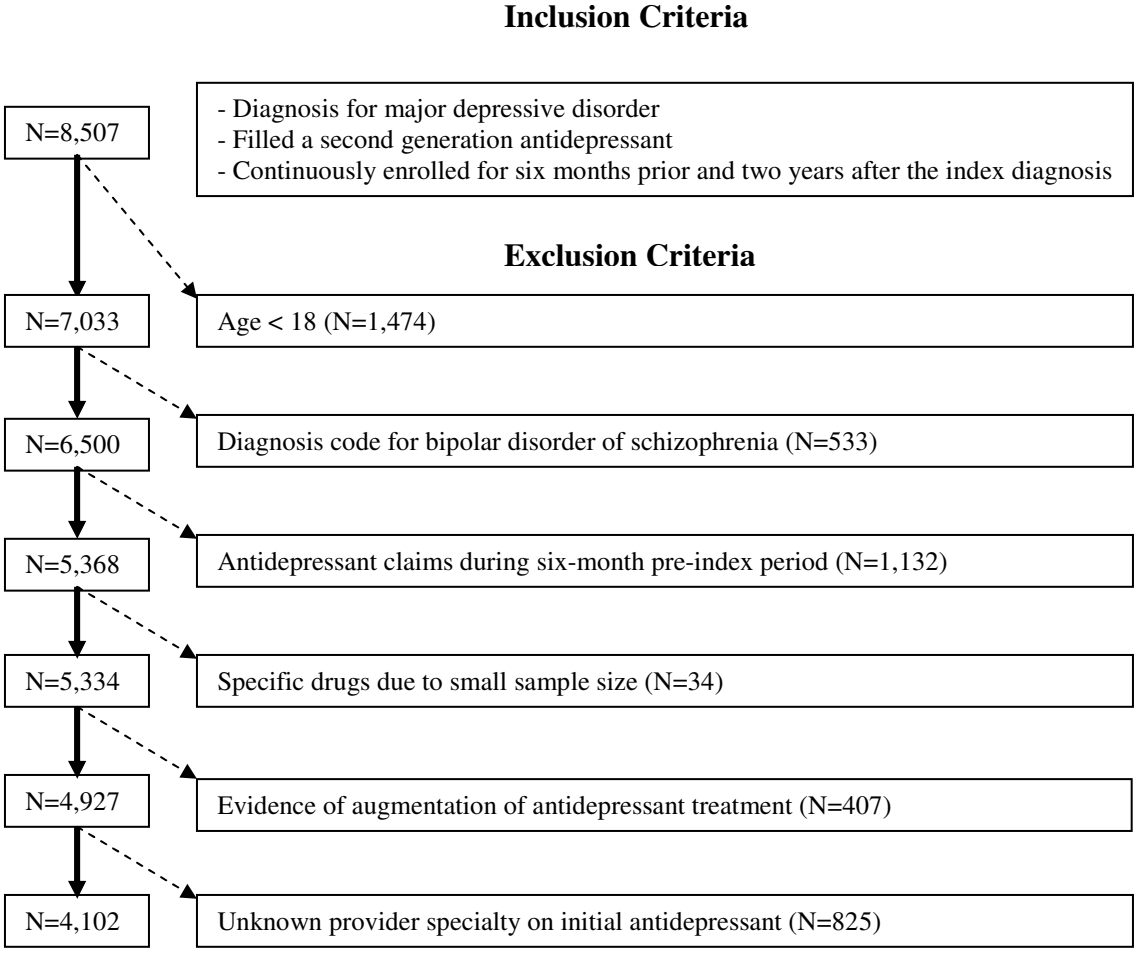
Figure 3.1 Follow-up Design



These four inclusion criteria yielded a sample of 8,570 subjects (Figure 3.2). Several exclusion criteria were applied to obtain the final sample used in this dissertation. Patients under 18 years old were excluded (n=1,474) because antidepressant management for children and adolescents is different from adults. Individuals were excluded from the analysis if they had an ICD-9 diagnosis code of bipolar disorder or schizophrenia (295.xx, 296.0x, 296.4x, 296.5x, 296.7X, 296.89, 296.80) because these mental health conditions might compromise their ability to take medication (n=533). To ensure that patients were newly started on the current course of antidepressant treatment (naïve users), patients could not have received an antidepressant prescription in the 6-month pre-index period (n=1,132). This new-user design eliminated prevalent user bias by restricting study population to persons under observation at the start of current course of treatment.[81]

We restricted the sample further to enrollees taking the following second generation antidepressants: bupropion, citalopram, escitalopram, fluoxetine, mirtazapine, paroxetine, sertraline, and venlafaxine, which were commonly prescribed in this sample and have better safety profiles than first-generation antidepressants. Patients prescribed trazodone, fluvoxamine, nefazodone, and a specific formulation of fluoxetine (Sarafem®, Warner Chilcott, Rockaway, NJ) were excluded because their sample size was too small (n=34). Patients who had evidence of overlapping supply of another antidepressant which indicates augmentation of the treatment were excluded, because antidepressant use was based on prescription refill records and might not be estimated accurately with augmentation (n=407). In other words, the dissertation focuses on mono-therapy users. Finally, patients with unknown provider specialty in their index antidepressant prescription claim were excluded because the provider type was the independent variable of interest (n=825). The final sample consists of 4,102 antidepressant users aged more than 18 years old with an MDD diagnosis.

Figure 3.2 Sample Selection



3.3 Variables

This section describes the definition and identification of several key variables that serve as dependent or main independent variables in specific aims, followed by a description of control variables.

3.3.1 Provider Specialty

Provider specialty is the independent variable of interest of this dissertation. The index antidepressant prescription claim for each patient was the first antidepressant prescription after the initial diagnosis of MDD. The provider specialty was identified for each patient based on the specialty of the provider of this first antidepressant prescription. We used prescription as the source of provider specialty because we assumed that patients received this initial antidepressant prescription from the providers who initiated and subsequently managed their antidepressant therapy. In a test of this assumption, we found that only 5% of patients received subsequent antidepressant prescriptions from different types of providers. The provider specialty was categorized into three mutually exclusive groups: a) primary care providers (PCP) include providers with specialties of family practice, internal medicine, obstetrics/gynaecology, pediatrics, and geriatrics; b) psychiatrists; c) non-psychiatric specialists (e.g. cardiologist, gastroenterologist, and oncologist).

3.3.2 Receipt of Guideline-concordant Follow-up Visits

Receipt of guideline-concordant follow-up visits is the first of two outcome variables in aim 2 and was constructed based on the Healthcare Effectiveness Data Information Set (HEDIS) measures.[12] Follow-up visits were identified by outpatient service claims with a non-mental health practitioner or mental health practitioner coded with a mental health diagnosis. Mental health diagnosis was defined with ICD-9 codes 210 to 319 inclusive, based

on any diagnosis field. Patients were considered to have guideline-concordant follow-up visits if they 1) received at least three follow-up visits during the first 90 days since the index antidepressant prescription (acute phase), AND 2) had at least one of the three follow-up visits with a prescribing practitioner (e.g., licensed physician, physician assistant, or other practitioner with prescribing privileges).

To evaluate whether the criteria used in HEDIS with any mental health diagnosis to be too inclusive, we descriptively examined the distribution of the diagnosis code on the visits identified. We found 84% of the claims had a depression-related mental health diagnosis.

3.3.3 Antidepressant Treatment Phases Completion

Antidepressant treatment phase completion is the second of two outcome variables in aim 2. Several methods have been developed to evaluate medication adherence (whether a patient takes a prescribed medication according to schedule) and persistence (whether a patient stays on therapy) using automated databases.[82] A successful completion of an antidepressant treatment phase requires adherence and persistency of the regimen. Such hybrid metrics are more stringent than adherence or persistency measurement alone and are preferred because of the tendency for claims data to overestimate medication use.[83]

Adherence was assessed using the medication possession ratio (MPR). MPR is defined using the continuous, multiple-interval medications available methodology, which has been widely used in assessment of medication use.[84] MPR is calculated as the sum of days-of-supply of all antidepressant prescriptions divided by the total number of days during the specified period. The formula for calculating MPR is specified as below:

MPR= (Sum of days of supply of prescriptions)/(Total number of days)

It is assumed perfect adherence during the days immediately preceding the end of acute phase (day 90). The over-supply of last refill in acute phase was carried to continuation phase. Patients who stayed in the hospital were assumed to be given the medication prescribed to them. Therefore, those days were considered as perfect adherence, and were added to the numerator of the MPR calculation. In addition, patients who switched antidepressants had their supply of the pre-switch medication truncated at the date when a different antidepressant medication was filled. MPR ranges from 0%, indicating no adherence to 100%, indicating perfect adherence. In the case of oversupply, MPR could be greater than 100%. We truncated MPR at 100%. Patient adherence was computed as a binary indicator. We used 80% as cut point based on prior literature.[82] Patients were assigned a score of 1 if they achieved an MPR greater or equal to 80%, or 0 if the MPR was less than 80%.

Persistency was measured as a function of gaps between refills.[85] Patients were classified as persistent if they had no evidence of a gap of more than half of the days-of-supply since the end of the last antidepressant prescription, which is based on clinical rationale from practicing psychiatrists and past studies.[86, 87] For example, a patient receiving prescription with a 30-day supply could have a gap between refills no longer than 45 days. Hence, only patients not having a gap and with at least 80% of MPR during the entire phase were deemed to have completed the phase.

Two dichotomous variables were created for antidepressant treatment. First, completion of acute phase (day 1 to day 90 since index antidepressant prescription claim) was defined for the whole population considering both MPR and gap. (Table 3.1) Ninety days was chosen based on guideline recommendations that acute phase regimen should last a minimum of 6-8 weeks and on average it takes 10-12 weeks to achieve full remission.[8, 9]

Next, for the sub-sample who completed acute phase, another variable of continuation phase (day 91 to day 270 since index antidepressant prescription claim) completion was defined based on MPR and gap. (Table 3.1) A period of 180 days was chosen to represent the average of recommended duration for continuation phase treatment (4-9 months).[8, 9]

Table 3.1 Definition of Completion of Antidepressant Treatment Phases

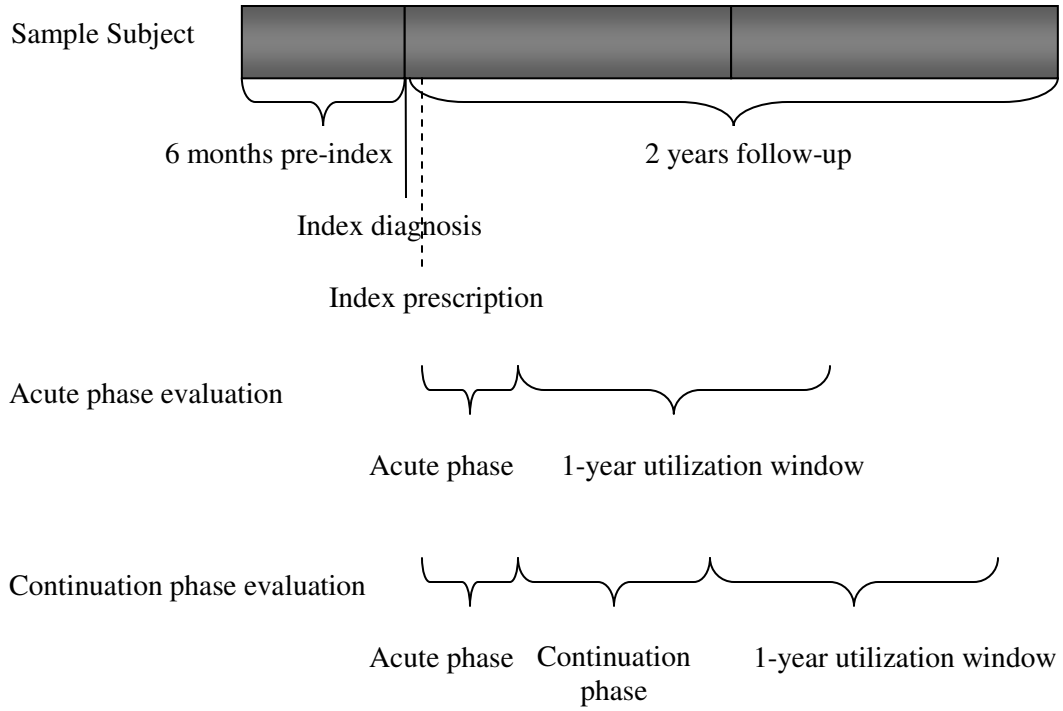
Antidepressant treatment phase	**Definition**
Complete acute phase	Patients having at least 72 days of antidepressant supply during the first 90 days period since first prescription refill (MPR≥80%), and not having a gap of more than 1.5 of the days-of-supply of previous antidepressant prescription between refills were deemed completed. Patients will be coded as completion=1 if met the above criteria, and 0 otherwise.
Complete continuous phase	Among patients who completed acute phase, those having at least 144 days of antidepressant supply during the first 180 days period since the completion of acute phase (MPR≥80%), and not having a gap of more than 1.5 of the days-of-supply of previous antidepressant prescription between refills were deemed completed. Patients will be coded as completion=1 if met the above criteria, and 0 otherwise.

3.3.4 All-cause and Mental Health-related Hospitalization/Emergency Room Visit

All-cause and mental health-related hospitalization and emergency room visits were the outcomes for Aim 3. We examined whether these events occurred in the one-year period after the end of the acute phase or the end of the continuation phase. For the model that assesses acute phase treatment, the one-year period begins at the end of acute phase and runs from day 91 to day 466 after the index antidepressant prescription (Figure 3.3). In the sub-sample of patients who completed acute phase and were assessed for continuation phase completion, the one-year period begins at the end of continuation phase and runs from day 271 to day 636 after the index antidepressant prescription (Figure 3.3). The purpose of examining the period after completion of a phase is to avoid simultaneity of the exposure

(completion of antidepressant treatment phase) and outcome (hospitalization/emergency room visit) measure.

Figure 3.3 Timeframe for Follow-up Period of Utilization



A binary variable was created to indicate whether a hospital admission or emergency room visit for any reason occurred in the one-year period for each individual. This variable represents all-cause utilization. Another binary variable was created for one or more all-cause hospitalizations. Binary variables for mental health-related utilization (hospital admission or emergency room visit) and hospitalization were also created, based on the ICD-9 codes 210 to 319 inclusive in any diagnosis field (Table 3.2).

Table 3.2 Definition of Outcomes in Aim 3

Variables	**Acute Phase**	**Continuation Phase**
	Examined Period	
	day 91 to day 466 since the index antidepressant prescription	day 271 to day 636 since the index antidepressant prescription
	Definition	
All-cause utilization	Hospital admissions or emergency room visits	Hospital admissions or emergency room visits
All-cause hospitalization	Hospital admissions	Hospital admissions
Mental health-related utilization	Hospital admissions or emergency room visits with ICD-9 codes 210-319 inclusive in any diagnosis field	Hospital admissions or emergency room visits with ICD-9 codes 210-319 inclusive in any diagnosis field
Mental health-related hospitalization	Hospital admissions with ICD-9 codes 210-319 inclusive in any diagnosis field	Hospital admissions with ICD-9 codes 210-319 inclusive in any diagnosis field

3.3.5 Control Variables

Control variables were chosen based on the conceptual framework from Chapter II including predisposing, enabling, need, treatment-related, and health insurance plan variables. Table 3.3 summarizes the control variables used for the analyses.

Table 3.3 Control Variables

Type of Variable	Variable	Type	Range/Categories
Predisposing	Age at diagnosis	Continuous	≥18
	Age categories	Categorical	18-34 (reference), 35-49, 50-64, ≥65
	Gender	Dichotomous	1=Male; 0=Female
	Region of residence	Categorical	east north central, east south central, middle Atlantic, mountain, New England, pacific, south Atlantic (reference), west north central and west south central
Enabling	Median household income in the state of residence	Continuous	$29,411-$54,535
	Percent of population with high school education in state of residence	Continuous	72.9%-88.3%
	Previous specialty care	Dichotomous	
Need	Hospitalization during pre-index period	Dichotomous	
	Chronic Disease Score	Continuous	0-8
	Comorbid anxiety	Dichotomous	
	Alcohol or substance abuse	Dichotomous	
	Received pregnancy-related visits	Dichotomous	
Treatment-related	Type of initial antidepressant	Categorical	bupropion, citalopram, escitalopram, fluoxetine (reference), mirtazapine, paroxetine, sertraline, and venlafaxine
	Complexity of daily antidepressant regimen	Dichotomous	Once daily (reference), ≥ 2 pills a day
	Quarter of year when initial antidepressant was prescribed	Categorical	first quarter of year (reference), second, third, and forth quarter of year
Health Insurance	Average 30-day antidepressant copayment	Continuous	$0-$196, median=$17
	30-day copayment categories	Categorical	$0-$10, $11-$15, $16-$20, >$20 (reference)
	Copayment for primary care visits	Continuous	$0-$111, median=$11
	Copayment for primary care visits categories	Categorical	$0 (reference), $1-$10, $11-$20, >$20
	Initial provider reimbursed on a capitated basis	Dichotomous	

Predisposing variables available in the data are age at diagnosis, gender, and region of residence (east north central, east south central, middle Atlantic, mountain, New England, pacific, south Atlantic, west north central and west south central). Age presented in the model in categorical forms (18-34 [reference], 35-49, 50-64, and ≥65).

Because there was no individual socio-economic status available in the data, we constructed median household income of the residing state as a proxy for economic status,[88] and percentage of population 25 years or older with high school degree of the residing state as a proxy for education level.[89] These are important patient socio-demographic variables from Andersen's Behavioral Model.

A binary variable indicating whether patients received any specialty care during the 6-month pre-index period was included as a proxy for specialty care access as well as patients' preference toward specialty care. Specialty care was defined based on provider specialty on the service claim including immunology, dermatology, neurology, psychiatry, urology, cardiology, gastroenterology, hematology, nephrology, rheumatology, endocrinology, oncology, pulmonary, infectious disease, ophthalmology, podiatry, and audiology.

Several need variables were constructed because they are the most immediate reasons for healthcare utilization based on Andersen's Behavioral Model. An indicator variable was created if a patient had any hospitalization during pre-index period. This variable served as an important proxy for health status as events like hospitalization usually indicate worse health. Inclusion of measure of comorbidity is important to adjust for patient case-mix. Several comorbidity measures have been shown to predict mortality or hospitalization.[90] The Chronic Disease Score (CDS)[91] is a medication-based risk-adjustment measure based on age,

gender, and history of dispensed drugs and it has empirically shown to predict comorbidity.[92, 93] Medical service claims in 6-month pre-index period were examined to identify conditions. Anxiety and substance abuse are common comorbid conditions for depression. Indicators for pre-existing anxiety (ICD-9 code in 300.00 or 300.02) and alcohol/substance abuse (ICD-9 in 303.xx-305.xx) were created to capture the mental health status of these patients. Psychological illness is an important confounding variable, and these mental health condition indicators may partially control for it. An indicator of pregnancy was created if the patient had any pregnancy-related outpatient visits based on ICD-9 code V22.xx or V23.xx in any diagnosis field to control for potential pregnancy in statistical models for Aims 2 and 3. This variable was included because pregnancy may influence the decision to prescribe or use an antidepressant and the outcome of all-cause hospitalization.

Treatment-related variables were also controlled for. Initial antidepressants including, bupropion, citalopram, escitalopram, fluoxetine, mirtazapine, paroxetine, sertraline, and venlafaxine were adjusted in the model to account for different side effect profiles that may influence the decision to continue/switch antidepressant therapy and the need for follow-up visits. The number of pills for daily doses was also included as an indicator for the complexity of the antidepressant regimen. Quarter of year when the initial antidepressant was prescribed was included in the models to control for seasonality differences.

Several variables were created for health plan characteristics. The full benefit structure of out-of-pocket payment and reimbursement scheme (fee-for-service or capitation) was not available. We constructed several proxies based on aggregated claims level information. Out-of-pocket copayment for a 30-days antidepressant prescription and out-of-pocket copayment for primary care provider visits were included as proxies for barriers of

access to care. All cost data has been adjusted for inflation to 2004 value using Consumer Price Index for medical care.[94] We also examined the reimbursement scheme of patient's initial prescriber specialty. Majority of providers were reimbursed based on fee-for-service. Small number of patients provider was reimbursed based on both fee-for-service and capitation basis. We created a binary indicator variable if more than 40% of claims for initial prescriber specialty during the whole study period were reimbursed on a capitated basis. 40% was chosen based on the median of individuals who had both claims reimbursed based on fee-for-service and capitation.

3.4 Statistical Models by Aim

This section describes the statistical models utilized in each aim. Table 3.4 summarizes the statistical models. Data construction was conducted using SAS 9.1 (Cary, NC), and statistical models were run using STATA 9.0 (College Station, TX).

Table 3.4 Summary of the Statistical Models

	Aim 1	**Aim 2**		**Aim 3**
Dependent variable **Independent variables**	Initial prescriber specialty	Guideline-concordant follow-up visits	Acute/ continuation phase completion	All-cause and mental health-related utilization/ hospitalization
Initial Prescriber Specialty		X	X	X
Receipt of guideline-concordant follow-up visits			X	
Acute phase/continuation phase completion				X
Predisposing variables				
Age at diagnosis	X	X	X	X
Gender	X	X	X	X
Region of residence	X	X	X	X
Enabling variables				
Median income in state of residence	X	X	X	X
% with high school education in state of residence	X	X	X	X
Prior specialty care	X			
Need variables				
Chronic disease score	X	X	X	X
Anxiety	X	X	X	X
Alcohol or substance abuse	X	X	X	X
Pregnancy-related visits		X	X	X
Prior hospitalization				X
Treatment-related variables				
Type of initial antidepressant		X	X	X
Complexity of daily regimen			X	
Quarter of year when initial antidepressant prescribed		X	X	X
Health insurance plan variables				
30-days antidepressant copayment			X	
Copayment for primary care visit	X	X		
Initial provider reimbursed on capitated basis		X		

3.4.1 Aim1

To examine characteristics among patients initially prescribed an antidepressant by providers with different specialties to treat major depressive disorder (MDD)

This aim examines patient characteristics among those who received an initial antidepressant prescription from different types of providers. Subjects were categorized into three groups based on their initial prescriber: PCPs, psychiatrists, and non-psychiatric specialists. A descriptive analysis of patient characteristics was conducted to examine unadjusted differences by initial prescriber specialty to inform analyses in Aims 2 and 3. Pearson's Chi-squared tests were used to determine whether categorical variables were different between groups, and analysis of variance (ANOVA) was used to examine the differences in continuous variables.

Since the outcome for this aim is un-ordered (PCP vs. psychiatrist vs. non-psychiatric specialist), multinomial logit model was used.[95] This model assumes that the alternatives are independently irrelevant. The probabilities for the three alternatives for a decision maker with characteristics x_i are

$$\Pr(Y_i = j|x_i) = \frac{e^{\beta_j' x_i}}{1 + \sum_{k=0}^{2} e^{\beta_k' x_i}} \quad \text{for } j=0,1,2$$

The log-likelihood can be derived by defining, for each individual, $d_{ij}=1$ if alternative j is chosen by individual i, and 0 if not, for the possible outcomes.

$$\ln L = \sum_{i=1}^{n} \sum_{j=0}^{J} d_{ij} \ln \Pr(Y_i = j)$$

Estimation of models is based on the method of maximum likelihood. Robust variance estimator was used for all regressions in this dissertation to account for heteroskedasticity.[96, 97]

The specification of this model is as follows:

$Pr\ (initial\ prescriber\ specialty) = \alpha + \beta_1 * AGE + \beta_2 * MALE + \beta_3 * REGION + \beta_4 * INCOME + \beta_5 * EDUCATION + \beta_6 * PRIOR\_SPECIALTY + \beta_7 * CDS + \beta_8 * ANXIETY + \beta_9 * SUBSTANCE + \beta_{10} * COPAY + \varepsilon$

Where *Pr (initial prescriber specialty) =0 if PCP; 1 if psychiatrist; 2 if non-psychiatric specialist*

AGE = vector of age categories

MALE = indicator variable for male gender

REGION = vector of region indicator variables

INCOME = median household income of the residing state in per $1,000

EDUCATION = % population with high school education of the residing state

PRIOR_SPECIALTY = indicator of any specialty care in pre-index period

CDS = Chronic disease score

ANXIETY = indicator variable for comorbid anxiety in pre-index period

SUBSTANCE = indicator variable for substance abuse in pre-index period

COPAY = vector of indicator variables for copayment level for primary care visits

Demographic and clinical characteristics where included a priori based on information in the literature.[7, 13, 43, 46-48] Demographic and socioeconomic variables include age, gender, region, and median household income and percentage of population with high school education of the residing state.[46] Use of specialty care in pre-index period was included to adjust for patient attitudes toward specialty care, access to specialty care, and established relationship between patients and specialists. Any prior use of specialty care is hypothesized to predict choosing specialists as their initial prescribing provider for MDD.

Chronic disease score serves as a proxy for health status using overall comorbid conditions, and is hypothesized to be a strong predictor for receiving care from specialists. Pre-existence of comorbid mental health conditions including anxiety and substance abuse may indicate the need for mental health specialty care, and is hypothesized to predict care from a psychiatrist. The copayment for PCP visits was included to proxy barriers to care. Out-of-pocket copayment for PCP visits was constructed to serve as a baseline burden a patient face for health service use because there is no information on the premium, copayment, or coinsurance of the study population.

The results were presented as odds ratios. The results from this model inform what variables differ among patients initially prescribed an antidepressant by different types of providers. The knowledge is important to identify potential confounders of provider effects in Aims 2 and 3.

3.4.2 Aim 2

To examine the association of antidepressant treatment with initial prescriber specialty and receipt of guideline-concordant outpatient follow-up visits among patients with MDD

3.4.2.1 Receipt of guideline-concordant outpatient follow-up visits varies by initial prescriber specialty

3.4.2.1.1 Analysis of Outpatient Follow-up Visits

This aim examines how the probability of receipt of guideline-concordant outpatient follow-up visits during the acute phase differs by the specialty of the provider prescribing the index antidepressant. First, the frequency of total number of visits during acute phase (90 days since index antidepressant prescription) was examined by initial prescriber specialty groups, followed by the proportion that received guideline-concordant of outpatient follow-up visits (at least three mental health-related visits and at least one visit made to provider with prescribing privileges). The mean number of follow-up visits during acute phase was compared between provider specialty groups using two-tailed student t-tests and the proportion that achieved guideline-concordant follow-up visits was compared between provider specialty groups using Pearson's Chi-square statistics.

The outcomes examined in this aim are discrete, and discrete dependent-variable models can be viewed as a reflection of an underlying utility function.[95] There is a latent variable y* such that

$$y^* = x'\beta + \varepsilon$$

Latent y* is unobserved. Instead, the observation is

y=1 if $y^* > 0$

y=0 if $y^* \leq 0$

For this type of binary outcome, a logit model can be estimated with a logistic distribution.[95] The logistic model assumes that 1) the logit link function is correct, 2) the relation between dependent variable and independent variables are linear and all necessary predictors are in the model, and 3) observations are independent. Maximum likelihood estimation is used assuming the logistic distribution of the dependent variable. The likelihood function for maximization is:

$$L = \prod_{i=1}^{n} \left(\frac{1}{1+e^{-X\beta}}\right)^{y_i} \left(\frac{e^{-X\beta}}{1+e^{-X\beta}}\right)^{1-y_i}$$

with X as all covariates and β as the coefficients.

The model of this aim is specified as follows:

Pr *(receipt of guideline-concordant outpatient follow-up visits)* $= \alpha + \beta_1 * PROVIDER + \beta_2 * AGE + \beta_3 * MALE + \beta_4 * REGION + \beta_5 * INCOME + \beta_6 * EDUCATION + \beta_7 * CDS + \beta_8 * PREGNANCY + \beta_9 * ANXIETY + \beta_{10} * SUBSTANCE + \beta_{11} * COPAY + \beta_{12} * CAPITATED + \beta_{13} * ANTIDEPRESSANT + \beta_{14} * QUARTER + \varepsilon$

Where *Pr (receipt of guideline-concordant outpatient follow-up) = 1 if patient had 3 or more mental health-related visits and at least one of the three visits was made to providers with prescribing privileges during 90 days since index antidepressant prescription; 0 otherwise*

PROVIDER = vector of provider specialty indicator variables

AGE = vector of age categories

MALE = indicator variable for male gender

REGION = vector of region indicator variables

INCOME = median household income of the residing state in per $1,000

EDUCATION = % population with high school education of the residing state

CDS = Chronic disease score

PREGNANCY = indicator variable for pregnancy-related visits during acute phase

ANXIETY = indicator variable for comorbid anxiety in pre-index period

SUBSTANCE = indicator variable for substance abuse in pre-index period

COPAY = vector of indicator variables for copayment level for primary care visits

CAPITATED = indicator that the initial provider received capitated reimbursement

ANTIDEPRESSANT = vector of indicator variables for initial antidepressant

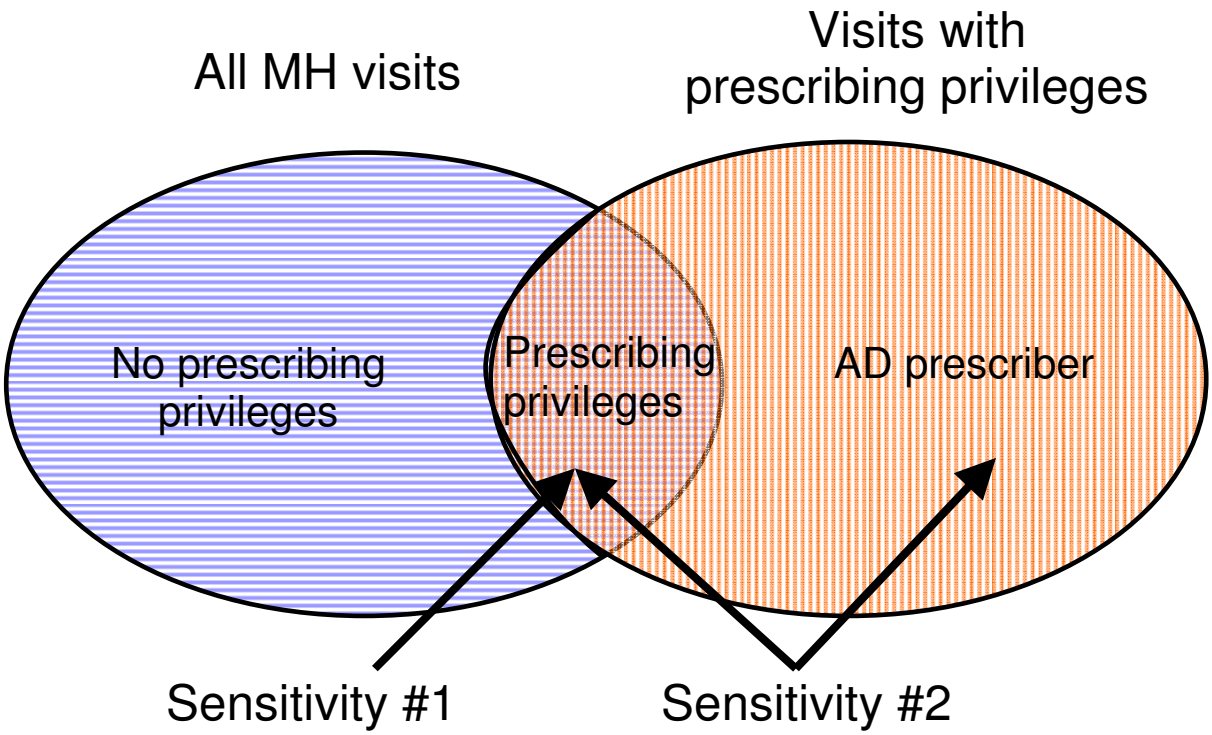
QUARTER = vector of indicators for quarter of year when treatment was initiated

PROVIDER represents a vector of provider specialty variables, including a PCP as initial prescriber (reference group), a psychiatrist as initial prescriber, and a non-psychiatric specialist as initial prescriber. These variables are the independent variables of interest. Sociodemographic variables such as age, gender, region of residence, and proxy of income and education were included as some were found to be significantly associated with follow-up visits.[4, 6] Chronic disease score, pregnancy, pre-existing anxiety and substance abuse were included because they might affect what types of provider they go to (e.g. the need for specialty care) and tendency to go for outpatient follow-up visits (e.g. the need for more frequent visits). Health plan characteristics included in the model were copayment for primary care visits and whether the patient saw an initial prescriber who was paid on a capitated basis. Higher out-of-pocket copayment that patients face might impose a burden on making medical visits. Capitated reimbursement provides incentive for providers to schedule medical visits less frequently.[6] Inclusion of these variables controls for cost containment on both patients and providers. Initial antidepressant was included in the model to control for potential differences in side effect profile that may result in more outpatient visits.[6] Quarter of year when the treatment was initiated to also control for seasonality. The results were presented with odds ratios.

3.4.2.1.2 Sensitivity Analyses

Sensitivity analysis is a useful tool to understand how study results may change according to certain parameters or definitions. For this research question, two sensitivity analyses were conducted to examine how provider specialty differences might change by varying the approaches to identify follow-up visits.

Figure 3.4 Illustration of Sensitivity Analyses for Follow-up



Note: the figure does not represent the actual proportion of the visits

Figure 3.4 illustrates the approaches to identify follow-up visits. The main approach already described using HEDIS measure identifies all visits with a mental health diagnosis (circle with horizontal lines). However, some of the visits were made to providers without prescribing privileges such as a psychologist or a social worker. These providers are not able to change patient's antidepressant therapy. In the first sensitivity analysis, we only consider someone having adequate outpatient follow-up visits if they had three or more visits to providers with prescribing privileges.

There are several reasons why depression care may be not be coded correctly on the claim. A scenario called "code creep", which refers to coding for another higher reimbursed diagnosis in place of an actual but lower reimbursed diagnosis, might happen in practice. In research using administrative data, code creep might result in misclassification when

variables are constructed based on diagnosis fields. Mental health diagnoses are also commonly under-coded in primary care due to patient's stigma.[22] To address this possibility in the second sensitivity analysis, we linked the provider from antidepressant prescription claims to outpatient service claims based on encrypted provider identification. Those visits, regardless of diagnosis code, made to the same provider who wrote the initial antidepressant prescription were identified. These visits were added on top of the ones used in the first sensitivity analysis as the outcome in the second sensitivity analysis (circle with vertical lines).

3.4.2.2 Completion of antidepressant acute and continuation phase varies by initial prescriber specialty

Aim 2 also examines whether completion of acute phase and continuation phase antidepressant treatment varies by initial prescriber specialty. Acute phase antidepressant use was measured based on prescription refill records during the first 90 days since index antidepressant prescription. Patients must have MPR ≥ 80% and no significant gap between refills to be considered as completed.[82] The same criteria were used to evaluate continuation phase completion during the 180 days after the acute phase for the sub-population who completed the acute phase. Descriptive analyses for independent variables were conducted between those who completed a phase versus those who did not using Pearson's Chi-squared tests for categorical variables and two-tailed student t-tests for continuous variables. The dependent variable is binary, so a logit regression was run for each phase.

3.4.2.2.1 Acute Phase

The acute phase model was specified as follows:

$$Pr(\text{completion of acute phase}) = \alpha + \beta_1 * PROVIDER + \beta_2 * FOLLOW\text{-}UP + \beta_3 * PSY * FOLLOW\text{-}UP + \beta_4 * AGE + \beta_5 * MALE + \beta_6 * REGION + \beta_7 * INCOME + \beta_8 * EDUCATION + \beta_9 * CDS + \beta_{10} * PREGNANCY + \beta_{11} * ANXIETY + \beta_{12} * SUBSTANCE + \beta_{13} * AD\_COPAY + \beta_{14} * DAILY\_PILL + \beta_{15} * ANTIDEPRESSANT + \beta_{16} * QUARTER + \varepsilon$$

Where *Pr (completion of acute phase) = 1 if patient completed acute phase; 0 otherwise*

PROVIDER = vector of provider specialty indicator variables

FOLLOW-UP = indicator variable for receipt guideline-concordant follow-up visits

*PSY*FOLLOW-UP = psychiatrist dummy and follow-up interaction*

AGE = vector of age categories

MALE = indicator variable for male gender

REGION = vector of region indicator variables

INCOME = median household income of the residing state in per $1,000

EDUCATION = % population with high school education of the residing state

CDS = Chronic disease score

PREGNANCY = indicator variable for pregnancy-related visits during acute phase

ANXIETY = indicator variable for comorbid anxiety in pre-index period

SUBSTANCE = indicator variable for substance abuse in pre-index period

AD_COPAY = vector of indicator variables for index antidepressant copayment level

DAILY_PILL = indicator variable for more than once-daily doses

ANTIDEPRESSANT = vector of indicator variables for initial antidepressant

QUARTER = vector of variables for quarter of year when treatment was initiated

The independent variable of interest is provider specialty variables (*PROVIDER*). We were also interested in whether patients who had guideline-concordant outpatient follow-up visits (*FOLLOW-UP*) were more likely to complete acute phase. An interaction term between the provider specialty variable and receipt of guideline-concordant follow-up visits (PSY*FOLLOW-UP) was included to account for any synergistic effects of care from psychiatrists and follow-up on acute phase completion. Based on the discussion in Chapter II, we do not consider non-psychiatric specialists differ from PCPs in knowledge and attitude toward depression treatment, so the interaction term between non-psychiatric specialist and follow-up was not included. Sociodemographic variables including age, gender, geographic region, and proxies for income and education at state level were included based on prior literature.[2, 4, 6, 13, 15, 16, 43] Chronic disease score was included to control for patient case-mix, even though it is unclear whether more comorbidities impose a burden to adhere or to increase the need for adherence.[2, 4, 6] Pre-existing anxiety serves as a need factor which is expected to be a positive predictor of adherence because antidepressants are also indicated to treat anxiety.[4, 16, 43] Substance abuse in the pre-index period was included because it is a comorbidity of depression and might impose a burden to antidepressant adherence.[2] Copayment for antidepressant prescriptions was included as a health plan characteristics. Higher copayments might discourage patients from refilling prescriptions.[98] Initial antidepressant type entered the model to control for potential differences in side effects that may result in discontinuation of treatment.[2, 6, 13, 15, 17] Number of pills of daily antidepressant doses was controlled for because the complexity of regimen might result in difficulties for patients to comply with treatment.[79] Finally, quarter of year when the antidepressant treatment was initiated was included to control for any seasonal effect.

Since the logistic regression model included an interaction term, the interpretation of odds ratio is not straight forward. Hence, the results were presented as marginal effects using the average of the probabilities method. The significance of the interaction term was examined using methods developed by Norton et al.[99, 100] To address the simultaneous nature and potential correlation between the error terms in guideline-concordant follow-up visits model and acute phase antidepressant completion model, a seemingly unrelated regression was run with bivariate probit model to examine the correlation.[95]

3.4.2.2.2 Continuation Phase

The continuation model was run on the sub-sample who completed acute phase (n=1,921). The dependent variable was a binary outcome of continuation phase completion. The specification of most of the independent variables was similar to the acute phase model. The interaction terms between provider specialty dummies and follow-up were not included because of the time lag between initial prescriber specialty and continuation phase (3 months). We also tested with inclusion of interaction term, but it was not significant. To assess whether the impact of follow-up visits in the acute phase was carried over to the continuation phase or if the follow-up visits during the continuation phase might be associated with antidepressant completion, we tested the correlation between number of follow-up visits in acute phase and number of follow-up visits in continuation phase. A high correlation of 0.68 was found. We also tested several different specifications for follow-up in the continuation phase because there are no guideline-recommended intervals. We examined continuous, binary (<3 vs. ≥3 visits), and categorical forms (0 visit, 1-2 visits, and 3 or more visits). The specification tests showed that the binary form was more appropriate (Appendix 3).

3.4.3 Aim 3

To examine the association of subsequent healthcare utilization with initial prescriber specialty and antidepressant treatment among patients with MDD

This aim examines how initial prescriber specialty and antidepressant treatment completion may associate with subsequent healthcare utilization. There were four binary outcomes identified during the one-year follow-up after a phase was completed: 1) all-cause utilization (hospitalization and emergency room visits), 2) all-cause hospitalization, 3) mental health-related utilization, and 4) mental health-related hospitalization.

3.4.3.1 Healthcare Utilization in the One-year Period after Acute Phase

A descriptive analysis for independent variables was conducted between those who had all-cause utilization (any hospitalization or emergency room visits) in the one-year period after the acute phase. Similar descriptive analyses were conducted for all-cause hospitalization, mental health-related utilization, and mental health-related hospitalization (See Table 3.2 for definition). Differences in categorical variables were tested with Pearson's Chi-squared test and two-tailed student t-tests were used for continuous variables.

Four logistic regressions were run to understand the influence of provider specialty and completion of acute phase antidepressant treatment on subsequent healthcare utilization. The dependent variable of the first regression was all-cause utilization. The second model was run with mental health-related utilization as the dependent variable with the same model specification. The third and forth models replaced utilization with all-cause hospitalization and mental health-related hospitalization, respectively.

The specification of the first model is:

$Pr\ (all\text{-}cause\ utilization) = \alpha + \beta_1 * ACUTE + \beta_2 * PROVIDER + \beta_3 * AGE + \beta_4 * MALE + \beta_5 * REGION + \beta_6\ INCOME + \beta_7 EDUCATION + \beta_8 * PREGNANCY + \beta_9 * PRIOR\_HOS + \beta_{10} * CDS + \beta_{11} * ANXIETY + \beta_{12} * SUBSTANCE + \beta_{13} * QUARTER + \varepsilon$

Where *Pr (all-cause utilization) = 1 if patient has all-cause hospitalization or emergency room visits; 0 otherwise,*

ACUTE = binary acute phase completion variable

PROVIDER = vector of provider specialty indicator variables

AGE = vector of age categories

MALE = indicator variable for male gender

REGION = vector of region indicator variables

INCOME = median household income of the residing state in per $1,000

EDUCATION = % population with high school education of the residing state

PREGNANCY = indicator variable for pregnancy-related visits during acute phase

PRIOR_HOS = indicator variable for prior hospitalization in pre-index period

CDS = Chronic disease score

ANXIETY = indicator variable for comorbid anxiety in pre-index period

SUBSTANCE = indicator variable for substance abuse in pre-index period

QUARTER = vector of variables for quarter of year when treatment was initiated

The dependent variable in the first model is a binary variable indicating the presence of any all-cause hospitalization/emergency room visits during the one-year period after acute phase. *Acute phase completion* (*ACUTE*) is a binary variable with non-completion as reference. *PROVIDER* is a vector of provider specialty variables in the model to test whether

patients initially prescribed an antidepressant by psychiatrists or by non-psychiatric specialists used more healthcare resources. Differences in utilization have been found in different socio-demographic groups, so these variables were included in the model.[18, 19] Since the all-cause utilization identified did not distinguish the reason for hospitalization and inpatient service for birth delivery is not considered an adverse event, an indicator variable of pregnancy-related outpatient visits during acute phase was included in the model to adjust for it. Without such adjustment, the effect of acute phase completion might be confounded if patients who were pregnant were more likely to terminate the treatment while having an inpatient service for birth delivery during the follow-up period. Other risk variables such as prior hospitalization, chronic disease score, anxiety, and substance abuse based on history in 6-month pre-index date period were included to adjust for case-mix.[18, 19] Quarter of year when the antidepressant treatment was initiated was included to control for any seasonal effect.

3.4.3.2 Healthcare Utilization in the One-year Period after Continuation Phase

Healthcare utilization in the year following the continuation phase was considered by those who completed the acute phase and had continuation phase antidepressant treatment. (n=1,921) A descriptive analysis for independent variables was conducted between those who had utilization (any hospitalization or emergency room visits) during one-year of follow-up after continuation phase versus those who did not. Similar descriptive analyses were conducted for all-cause hospitalization, mental health-related utilization, and mental health-related hospitalization.

Four logistic regressions were run on the sub-sample who completed acute phase to understand the influence of initial prescriber specialty and completion of continuation phase.

The dependent variable of the first regression was all-cause utilization. Three similar models were run with all-cause hospitalization, mental health-related utilization, and mental health-related utilization as dependent variables respectively. The specification of independent variables was similar to the acute phase model. The results were presented with odds ratios.

3.5 Specification Tests

A Hausman test was performed to examine whether the assumption of independence of irrelevant alternatives (IIA) for multinomial logit model holds for the Aim 1 model.[101] The test evaluates the significance of an estimator (multinomial logit model) versus an alternative estimator (logit model omitting an alternative in multinomial logit model). Robust standard errors were used for all logistic regression to adjust for heteroskedasticity. A diagnostic test for specification error using Stata command "linktest" was used after logistic regression models for Aim 2 and Aim 3.[102] It tests whether the logit of the outcome variable is indeed a linear combination of the independent variables and whether there is omitted variable misspecification. Model fit of the logistic regression was tested using the Hosmer and Lemeshow's goodness-of-fit test.[102] Multicollinearity among independent variables was tested using tolerance and variance inflation factor (VIF). C-statistics were also reported for logistic regression model to indicate the discriminative ability of the model. Results of specification tests for each analytical model are presented in Appendix 4.

3.6 Power Analysis

Power analyses were conducted for the models for Aim 2, and Aim 3 using STATA 9.0 (College Station, TX). Power calculation was based on two-sample comparison of proportions (Patients initially prescribed an antidepressant by PCPs and patients initially prescribed an antidepressant by psychiatrists). The parameters needed for power calculation are:

- Actual sample size of each group
- Proportion with positive response (Y=1) when X=0
- Proportion with positive response (Y=1) when X=1
- Alpha is the probability of rejecting a true null hypothesis.

Alpha was set as 0.05 for all power calculations.

3.6.1 Aim 2 Follow-up

For the model that estimated receipt of guideline-concordant follow-up visits, a power analysis was conducted to evaluate whether the model had power to detect differences between patients initially prescribed an antidepressant by PCPs and patients initially prescribed an antidepressant by psychiatrists. In this dissertation, we have a sample of 2,441 PCP patients (19% of whom received guideline-concordant follow-up visits) and 1,443 psychiatrist patients (52% of whom received guideline-concordant follow-up visits). We calculated the power with various levels of relative and absolute differences (Table 3.5). Our sample allows us to detect a relative 21% increase (an absolute 4% increase) with 83% of power.

Table 3.5 Power Analysis for Aim 2 Follow-up Model

Parameter Inputted for PCP Group (%)	Parameter Inputted for Psy Group (%)	Relative Increase (%)	Absolute Increase (%)	Power (%)
19	21	10	2	31
19	22	15	3	60
19	23	21	4	83
19	24	26	5	95
19	*52*	*174*	*33*	*100*

Note: row in italic is data from the sample

3.6.2 Aim 2 Acute Phase

A power analysis was conducted to test whether the model for acute phase completion has power to detect differences between patients initially prescribed an antidepressant by PCPs and patients initially prescribed an antidepressant by psychiatrists. We have a sample of 2,441 PCP patients (46% of whom completed acute phase) and 1,443 psychiatrist patients (48% of whom completed acute phase). We calculated the power with various levels of relative and absolute differences (Table 3.6). Our sample allows us to detect a relative 11% increase (an absolute 5% increase) with 84% of power.

Table 3.6 Power Analysis for Aim 2 Acute Phase Model

Parameter Inputted for PCP Group (%)	Parameter Inputted for Psy Group (%)	Relative Increase (%)	Absolute Increase (%)	Power (%)
46	*48*	*4*	*2*	*21*
46	49	7	3	43
46	50	9	4	66
46	51	11	5	84
46	52	13	6	94

Note: row in italic is data from the sample

3.6.3 Aim 2 Continuation Phase

A power analysis was conducted to test whether the model for continuation phase completion has power to detect differences between patients initially prescribed an antidepressant by PCPs and patients initially treated by psychiatrists. We have a sample of 1,129 PCP patients (45% of whom completed continuation phase) and 694 psychiatrist

patients (46% of whom completed continuation phase). We calculated the power with various levels of relative and absolute differences (Table 3.7). Our sample allows us to detect a relative 16% increase (an absolute 7% increase) with 82% of power.

Table 3.7 Power Analysis for Aim 2 Continuation Phase Model

Parameter Inputted for PCP Group (%)	Parameter Inputted for Psy Group (%)	Relative Increase (%)	Absolute Increase (%)	Power (%)
45	*46*	*2*	*1*	*6*
45	48	7	3	22
45	50	11	5	52
45	52	16	7	82
45	54	20	9	96

Note: row in italic is data from the sample

3.6.4 Aim 3 Acute Phase

It is of particular interest to understand whether models for psychiatric utilization/hospitalization were under-powered because those events were relatively rare. We have a sample of 2,441 PCP patients and 1,443 psychiatrist patients. We calculated the power with various levels of relative and absolute differences (Table 3.8). Our sample allows us to detect a relative 24% increase (an absolute 4% increase) with 86% of power for all-cause utilization, a relative 75% increase (an absolute 3% increase) with 87% of power for mental health-related utilization, a relative 43% increase (an absolute 3% increase) with 78% of power for all-cause hospitalization, and a relative 67% increase (an absolute 2% increase) with 86% of power for mental health-related hospitalization.

Table 3.8 Power Analysis for Aim 3 Acute Phase Model

Parameter Inputted for PCP Group (%)	Parameter Inputted for Psy Group (%)	Relative Increase (%)	Absolute Increase (%)	Power (%)
All-cause Utilization				
17	19	12	2	34
17	20	18	3	63
17	21	24	4	86
17	*22*	*29*	*5*	*96*
17	23	35	6	99
Mental Health-related Utilization				
4	5	25	1	12
4	6	50	2	57
4	*7*	*75*	*3*	*87*
4	8	100	4	99
4	9	125	5	100
All-cause Hospitalization				
7	*9*	*30*	*2*	*22*
7	10	43	3	78
7	11	57	4	96
7	12	71	5	100
7	13	86	6	100
Mental Health-related Hospitalization				
3	*4*	*33*	*1*	*47*
3	5	67	2	86
3	6	100	3	99
3	7	133	4	100
3	8	167	5	100

Note: row in italic is data from the sample

3.6.5 Aim 3 Continuation Phase

We have a sample of sample of 1,129 PCP patients and 694 psychiatrist patients in the continuation phase analyses. We calculated the power with various levels of relative and absolute differences (Table 3.9). Our sample allows us to detect a relative 50% increase (an absolute 4% increase) with 83% of power for all-cause utilization, a relative 60% increase (an absolute 3% increase) with 83% of power for mental health-related utilization, a relative 63% increase (an absolute 5% increase) with 87% of power for all-cause hospitalization, and

a relative 133% increase (an absolute 4% increase) with 91% of power for mental health-related hospitalization.

Table 3.9 Power Analysis for Aim 3 Continuation Phase Model

Parameter Inputted for PCP Group (%)	Parameter Inputted for Psy Group (%)	Relative Increase (%)	Absolute Increase (%)	Power (%)
All-cause Utilization				
16	*20*	*25*	*4*	*72*
16	21	50	5	83
16	22	100	6	93
16	23	125	7	97
16	24	150	8	99
Mental Health-related Utilization				
5	*6*	*20*	*1*	*45*
5	7	40	2	58
5	8	60	3	83
5	9	80	4	95
5	10	100	5	99
All-cause Hospitalization				
8	*9*	*13*	*1*	*5*
8	10	25	2	21
8	11	38	3	45
8	12	50	4	70
8	13	63	5	87
Mental Health-related Hospitalization				
3	*5*	*67*	*2*	*19*
3	6	100	3	70
3	7	133	4	91
3	8	167	5	98
3	9	200	6	100

Note: row in italic is data from the sample

3.7 Statistical Issue

3.7.1 Imbalance of Observable Variables

In a randomized-controlled experiment, randomization will guarantee the balance of observed and unobserved characteristics between groups and ensure that there are no systematic differences. In observational studies, however, the investigators have no control over a subject's group membership. There might be some systematic observed differences between group members. If such differences affect both the assignment of group membership and outcome of interest, failure to control for them will result in biased estimates. Since the patients in this dissertation were not randomly assigned to be treated by different types of providers, our analyses were subject to this issue. Several approaches have been used to control for imbalance in observed variables including matching, stratification, covariate adjustment via regressions, and propensity scores. In this dissertation, we used propensity score matching to adjust for imbalance of variables between patients who were initially prescribed an antidepressant by a PCP and patients who were initially prescribed an antidepressant by a psychiatrist.

3.7.1.1 Summary of Propensity Score

Propensity scores were first proposed by Rosenbaum and Rubin for confounder control in observational studies.[103] The propensity score for an individual is the probability that he or she will be assigned to the treatment group conditional on that individual's observed characteristics. A propensity score provides a scalar summary of the covariates which does not limit the number of covariates, unlike other methods for adjustment. Use of propensity score enables an observational study to appear to be "quasi-randomized" on observed variables for the groups. Ideally, pairing individuals with the same propensity score

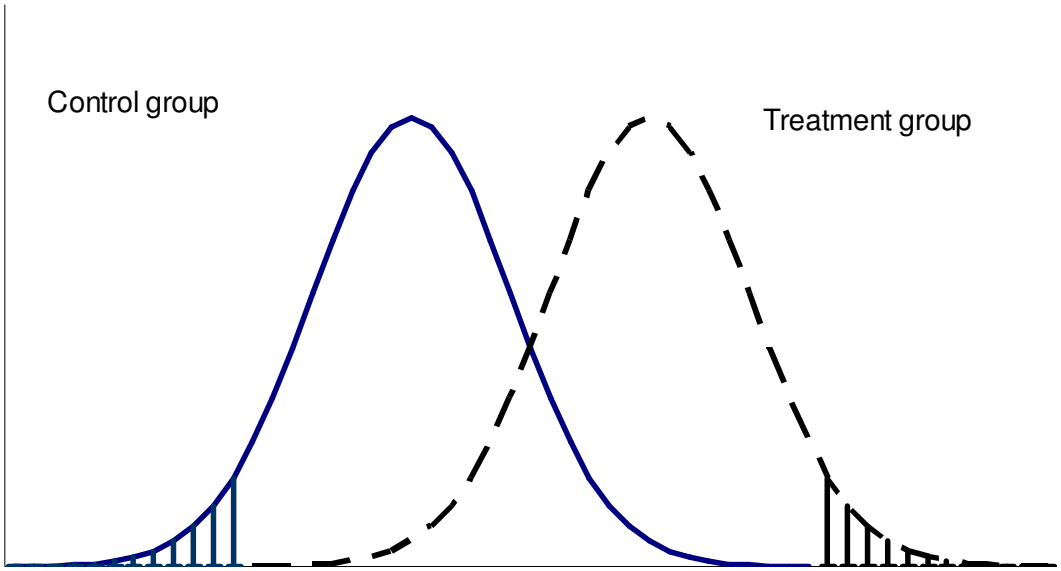
will, on average, lead to similar distribution of the observed characteristics, although the individual values of the characteristics may differ within paired groups.[104] The propensity score model should include confounders of exposure and outcome in the model to reduce bias.[105] In addition, it is suggested that variables that are unrelated to the exposure but related to the outcome should always be included in a propensity score model to decrease the variance of an estimated exposure effect without increasing bias.[106]

The three most commonly used techniques based on the propensity score to control for confounding are matching, stratification, and regression adjustment.[107] We chose to apply propensity score matching because a simulation study showed that propensity score matching resulted in least bias in estimating marginal odds ratios among the three approaches.[108] Matching based on propensity scores will obtain unbiased treatment effect estimates if several assumptions hold. The key assumptions are that all confounding covariates are observed and the model generating propensity scores is correctly specified.[103]

3.7.1.2 Propensity Score Matching Strategies

The treatment group tends to have a distribution with higher propensity to receive treatment, while the control group has a distribution with lower propensity to receive treatment (Fig 3.5). It is important to have enough overlap to be able to match a sufficient number of treatment and control group subjects. In this example, the subjects of upper tail of the treatment group and lower tail of the control group will be left out of the analyses because there are no exact matches.

Figure 3.5 Distribution of Propensity of Exposed and Unexposed Group



Several matching strategies has been proposed including 1) nearest available matching on the estimated propensity score, 2) Mahalanobis metric matching including the propensity score, 3) nearest available Mahalanobis metric matching within calipers defined by the propensity score, and 4) greedy matching.[104, 109] The following paragraph describes each method.

1) Nearest available matching on the estimated propensity score method randomly orders the treated and control subjects, then selects the first treated subject with the closet propensity score. They are removed from consideration after being matched.[104] 2) Mahalanobis metric matching uses several background covariates including the propensity score to calculate the Mahalanobis distance between treated and control subjects:

$$d(i, j) = (u - v)^T C^{-1} (u - v)$$

where u and v are values of the matching variables for the treated subject i and control subject j, and C is the sample covariance matrix of the matching variables from the full set of

control subjects. Subjects are randomly ordered, and the first treated subject will be matched based on the control with the smallest Mahalanobis distance from the treated subject's propensity score.[104] 3) Nearest available Mahalanobis metric matching within calipers defined by the propensity score combines the first two methods. The first treated subject is selected in a random order, and controls within a preset amount of the treated subject's propensity score are selected to calculate Mahalanobis distances based on a smaller number of covariates.[104] 4) Greedy matching utilizes a hierarchical sequence to make the "best" matches first and "next best" matches next will be used. The greedy matching procedure first identifies match-pairs within a closeness range of 0.00001 of the propensity score, then if not individuals can be found, next matched pairs in range of 0.0001 will be searched and so on up to a closeness range of 0.1. If more than one un-matched control matches to a case, the control will be selected at random. Once the match is made, the match is not reconsidered (without replacement).[109]

3.7.1.3 Diagnostic Test

The discrimination of the propensity score can be measured by the area under the receiver operating characteristics (ROC) curve or c-statistic.[110] The c-statistic will range between 0.5, indicating a model that performs no better than chance, and 1.0, indicating the ability to perfectly distinguish subjects. In addition, standardized differences, which is insensitive to sample size, can be calculated to examine the balance of covariates.[111] Standardized differences are calculated as follows:

$$d = \frac{100 \times \left| \bar{x}_{treatment} - \bar{x}_{control} \right|}{\sqrt{\frac{s^2_{treatment} + s^2_{control}}{2}}}$$

where x is the sample mean and s is the sample standard deviations of covariates, respectively. Standardized differences less than 20 are considered small differences.[112] Successful propensity score matching should significantly improved balance and achieve balance of all observable variables between groups.

3.7.1.4 Propensity Score Building for the Study Sample

In this dissertation, we matched the population based on the propensity score of whether they received an initial antidepressant from a psychiatrist as opposed to from a PCP. Patients initially prescribed an antidepressant by non-psychiatric specialists were excluded because they account for less than 5% of population and matching would be difficult for this group.

A propensity score model was built to predict the likelihood that patients are initially prescribed an antidepressant by psychiatrists as opposed to by primary care providers. The variables included in the propensity score models were potential confounders, and predictors of outcome or exposure. Major categories included socio-demographic characteristics (age, gender, region), health plan characteristics (primary care copayment), prior utilization (specialty care, psychotherapy, hospitalization, medication use), and proxies for physical and mental health status (comorbidities, chronic disease score). Interaction between variables was performed, and interaction terms which reached statistical significance ($p<0.05$) remained in the model. Table 3.10 presents the 41 variables included in the propensity score model. The associations and c-statistic were based on logit models of specialty of the initial provider with each variable entered one at a time. The model which included all variables resulted in an overall c-statistic of 0.716.

Table 3.10 Association between Patient characteristics and Initial Prescriber Specialty

Rank	Variable	OR	95% CI	c-statistics
1	Prior mental health specialty care	3.760	3.135-4.511	0.590
2	Age	0.980	0.974-0.985	0.570
3	Male	1.672	1.460-1.915	0.559
4	Prior psychotherapy	3.096	2.519-3.806	0.558
5	Prior mental health care x psychotherapy	3.065	2.484-3.782	0.555
6	Region (east north central)	0.585	0.502-0.681	0.551
7	Chronic disease score	0.941	0.867-1.020	0.535
8	Prior non-mental health specialty care	1.368	1.189-1.572	0.534
9	Region (west north central)	1.678	1.361-1.997	0.528
10	% with high school education in the state	0.987	0.966-1.008	0.525
11	Number of medication	0.988	0.970-1.007	0.522
12	Prior hospitalization	1.933	1.492-2.503	0.521
13	Region (west south central)	0.634	0.505-0.795	0.520
14	Time of diagnosis (forth quarter of year)	0.846	0.735-0.974	0.518
15	Positive primary care copay	0.677	0.769-0.999	0.516
16	Psychotropic agent	1.216	1.037-1.425	0.516
17	Anxiety	1.504	1.188-1.902	0.515
18	Region (mountain)	0.522	0.280-0.719	0.515
19	Substance abuse	1.629	1.194-2.222	0.510
20	Region (east south central)	0.610	0.432-0.861	0.510
21	Time of diagnosis (third quarter of year)	1.093	0.950-1.258	0.510
22	State median income in 1000	0.989	0.972-1.005	0.508
23	Hypertension	0.865	0.700-1.069	0.507
24	Region (pacific)	0.745	0.501-1.110	0.504
25	Region (new england)	1.226	0.859-1.751	0.503
26	Region (middle atlantic)	1.362	0.875-2.122	0.503
27	Chronic pulmonary disease	1.504	0.855-2.647	0.503
28	Headache and migraine	0.933	0.722-1.204	0.502
29	Congestive heart failure	0.281	0.063-1.257	0.502
30	Peripheral vascular disease	0.676	0.212-2.159	0.502
31	Hemiplegia	0.307	0.068-1.385	0.502
32	Dementia	2.543	0.717-9.027	0.501
33	Cerebrovascular disease	0.338	0.039-2.895	0.501
34	Connective tissue disease	0.704	0.247-2.002	0.501
35	Moderate or severe renal disease	2.374	0.752-7.495	0.501
36	Diabetes	0.945	0.614-1.455	0.501
37	Myocardial infarction	0.987	0.388-2.512	0.500
38	Mild liver disease	1.354	0.363-5.051	0.500
39	Metastatic solid tumor	1.693	0.238-12.03	0.500
40	Moderate or severe liver disease	0.967	0.283-3.308	0.500
41	Time of diagnosis (second quarter of year)	1.006	0.852-1.187	0.500

After the propensity scores were generated, patients initially prescribed an antidepressant by psychiatrists were matched to patients initially prescribed an antidepressant by PCPs. In a study comparing nearest available matching, Mahalanobis metric matching, and Nearest available Mahalanobis metric matching within calipers, Rosenbaum and Rubin concluded that the third technique produces the best balance between the covariates among the three matching strategies.[104] An empirical study comparing these methods also came to the same conclusion.[113] Therefore, we dropped the first two matching strategies from consideration. However, there has been no published comparison between greedy matching and nearest available Mahalanobis metric matching within calipers, so we conducted an analysis of the two matching techniques to identify the best method for our sample. The criteria for choosing strategy for matching were: 1) best balance of observed variables between groups via standardized differences, 2) maximum number of matches. The matching was conducted using SAS 9.1 (Cary, NC).

After applying greedy matching and nearest available Mahalanobis metric matching within calipers, the balance between controls and treated before and after matching is summarized in Table 3.11

Table 3.11 Pre-matching and Post-matching Comparison

	Pre-matching		Post-matching			
Matching Strategies			Greedy matching		Nearest available Mahalanobis metric matching within calipers	
Initial prescriber	PCP	Psychiatrist	PCP	Psychiatrist	PCP	Psychiatrist
Sample size	2,441	1,443	1,204	1,204	1,219	1,219
% psychiatrist group matched			83%		84%	
Mean PS	0.321	0.458	0.407	0.407	0.404	0.409
Minimum PS	0.007	0.100	0.096	0.100	0.099	0.100
Maximum PS	0.912	0.951	0.912	0.910	0.912	0.910

Greedy matching resulted in 83% of patients initially treated by psychiatrists being matched, and Mahalonobis matching with calipers resulted in 84% patients initially treated by psychiatrist being matched. Figure 3.6, 3.7 and 3.8 present the distribution of propensity scores of the original sample, post-matching sample based on greedy matching, and post-matching sample based on nearest available Mahalanobis metric matching within calipers, respectively.

Figure 3.6 Distributions of Propensity Score before Matching between Primary Care Provider and Psychiatrist Group

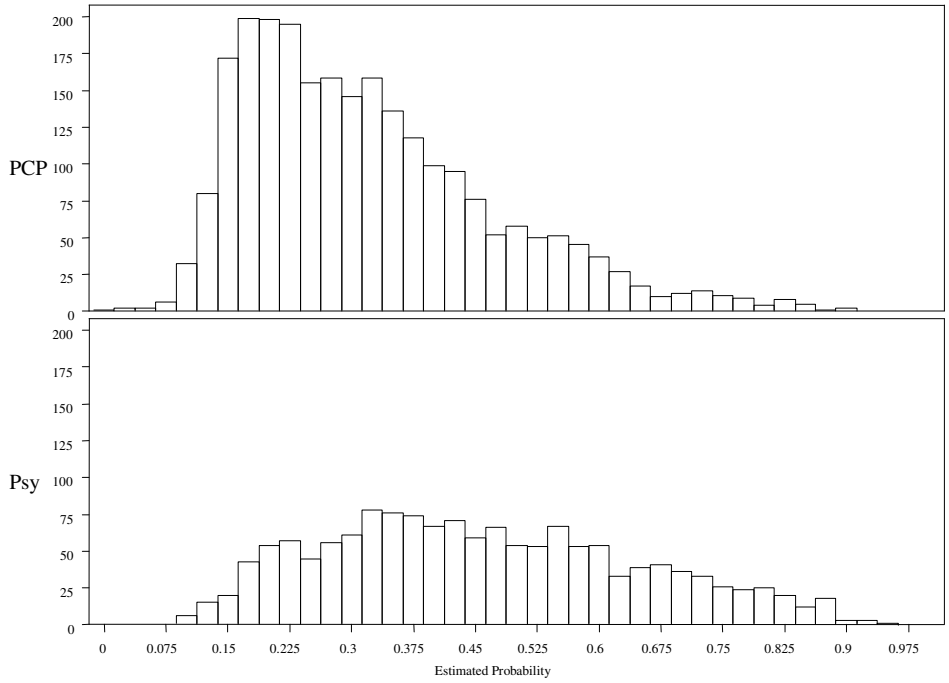


Figure 3.7 Distributions of Propensity Score after Greedy Matching between Primary Care Provider and Psychiatrist Group

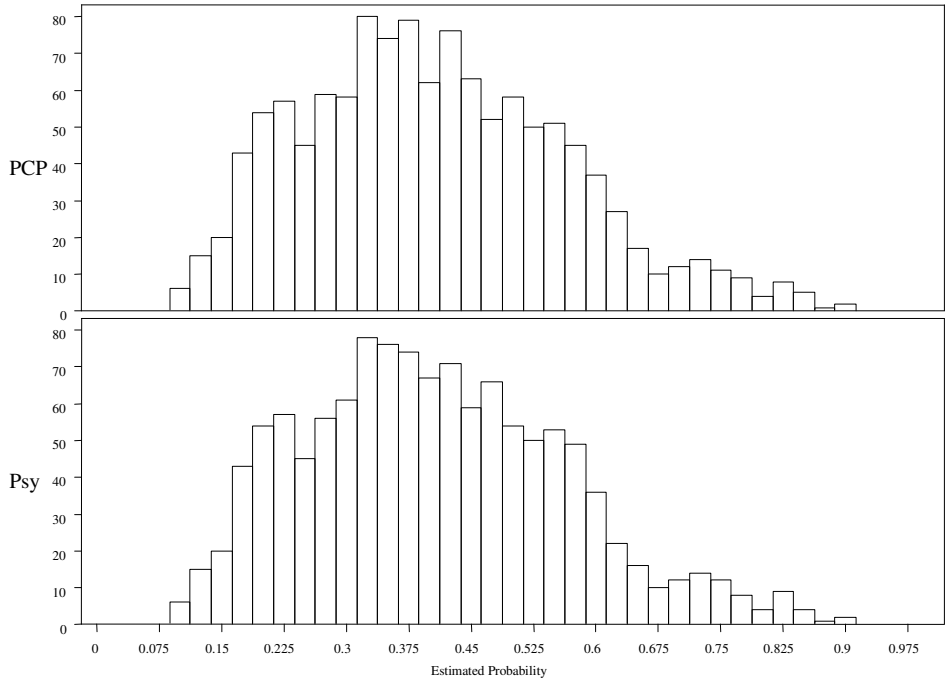
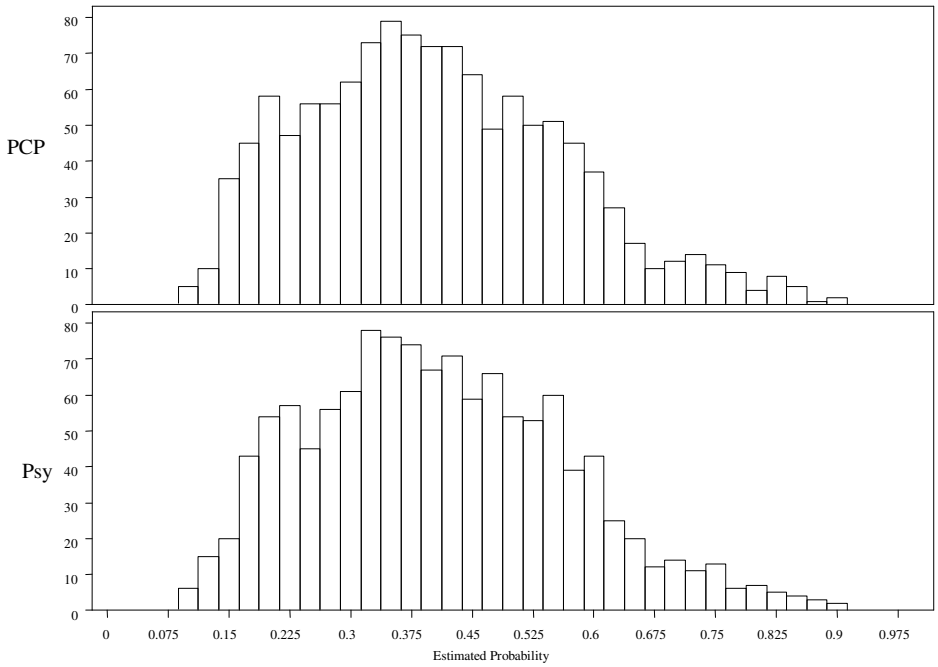


Figure 3.8 Distributions of Propensity Score after Mahalanobis Matching with Caliper between Primary Care Provider and Psychiatrist Group



By comparing the distribution of the propensity score between greedy matching and Mahalanobis matching with calipers in Table 3.10 and Figure 3.7 and 3.8, the post-matching distribution of propensity scores appeared to be similar between the two approaches. The balance between patient characteristics requires examination to choose which method to apply.

The differences in baseline characteristics before and after the match were examined to determine the performance of the match using two-tailed student t-test, Pearson's Chi-square statistics, and standardized differences. Table 3.12 summarizes the patient characteristics before and after matching.

Table 3.12 Patient Characteristics Before and After Propensity Score Matching

	Pre-matching				Post-greedy matching				Post-Mahalanobis matching with calipers			
Number of observations	PCP	Psy	P-value	Std Dif	PCP	Psy	P-value	Std Dif	PCP	Psy	P-value	Std Dif
	2,441	1,443			1,204	1,204			1,219	1,219		
% of sample	62.8	37.2			50.0	50.0			50.0	50.0		
Age	41.0 (11.8)	38.1 (11.9)	<0.001	24.33	39.0 (11.5)	39.0 (11.9)	0.848	0.78	39.2 (11.7)	39.0 (11.8)	0.605	2.09
Male (%)	30.4	42.2	<0.001	24.73	39.0	40.5	0.560	2.37	40.0	39.5	0.804	1.01
Region												
East North Central (%)	31.4	21.1	<0.001	23.52	22.9	23.9	0.564	2.35	24.5	23.8	0.670	1.72
East South Central (%)	5.1	3.2	0.005	9.70	3.2	3.3	0.909	0.47	3.0	3.3	0.641	1.89
Middle Atlantic (%)	1.8	2.5	0.170	4.47	2.4	2.2	0.787	1.10	2.4	2.6	0.697	1.58
Mountain (%)	6.7	3.6	<0.001	13.95	4.6	4.1	0.548	1.34	4.4	3.9	0.611	2.06
New England (%)	3.1	3.7	0.260	3.69	3.3	3.5	0.822	2.45	3.5	3.6	0.826	0.89
Pacific (%)	3.3	2.5	0.147	4.90	2.9	2.7	0.710	0.91	2.5	2.8	0.706	1.53
South Atlantic (%)	26.3	39.4	<0.001	28.32	36.3	36.0	0.865	1.51	37.2	37.4	0.900	0.51
West North Central (%)	10.4	16.0	<0.001	16.73	15.0	15.3	0.865	0.69	14.1	14.1	1.000	0.00
West South Central (%)	11.9	7.9	<0.001	13.48	9.3	9.1	0.832	0.86	8.5	8.5	0.942	0.29
Median household income of the residing state	41,656 (3,911)	41,479 (3,956)	0.175	4.50	41,591 (3,736)	41,541 (4,063)	0.754	1.28	41,602 (3,674)	41,512 (4,007)	0.564	2.34
% of population with high school education of the residing state	80.5 (3.3)	80.4 (2.8)	0.214	4.21	80.4 (3.0)	80.4 (2.8)	0.824	0.90	80.4 (3.0)	80.4 (2.8)	0.892	0.55
Use of mental health-related specialty care during pre-index period (%)	8.9	26.7	<0.001	48.12	16.9	17.2	0.828	0.88	17.0	17.9	0.557	2.38
Use of non-mental health-related specialty care during pre-index period (%)	28.2	34.9	<0.001	14.54	33.3	33.1	0.931	0.35	33.6	32.7	0.667	1.74
Prior psychotherapy (%)	6.8	18.4	<0.001	35.58	12.7	12.3	0.758	1.26	13.0	13.4	0.765	1.21
Myocardial infarct (%)	0.49	0.48	0.978	0.09	0.33	0.42	0.738	1.36	0.33	0.49	0.526	2.57
Congestive heart failure (%)	0.49	0.14	0.076	6.30	0.08	0.17	0.564	2.35	0.16	0.16	1.000	0.00
Peripheral vascular disease (%)	0.41	0.28	0.506	2.26	0.25	0.25	1.000	0.00	0.41	0.25	0.479	2.87
Dementia (%)	0.16	0.42	0.134	4.69	0.33	0.25	0.705	1.54	0.25	0.33	0.705	1.53

	Pre-matching				Post-greedy matching				Post-Mahalanobis matching with calipers			
Number of observations	PCP	Psy	P-value	Std Dif	PCP	Psy	P-value	Std Dif	PCP	Psy	P-value	Std Dif
Cerebrovascular disease (%)	0.20	0.07	0.299	3.66	0.08	0.08	1.000	0.00	0	0.08	0.317	4.05
Chronic pulmonary disease (%)	1.07	1.59	0.154	4.62	1.50	1.50	1.000	0.00	1.31	1.64	0.502	2.72
Connective tissue disease (%)	0.49	0.35	0.508	2.25	0.33	0.42	0.738	1.36	0.49	0.41	0.763	1.22
Mild liver disease (%)	0.20	0.28	0.650	1.48	0.25	0.17	0.654	1.82	0.16	0.16	1.000	0.00
Hemiplegia (%)	0.45	0.14	0.104	5.76	0.25	0.17	0.654	1.82	0.16	0.16	1.000	0.00
Moderate or severe renal disease (%)	0.20	0.48	0.128	4.78	0.25	0.33	0.705	1.54	0.25	0.33	0.705	1.53
Diabetes (%)	2.42	2.29	0.797	0.86	2.33	1.91	0.479	2.88	1.72	2.21	0.382	3.54
Any tumor (%)	1.07	0.69	0.242	3.99	0.50	0.83	0.316	4.09	0.98	0.82	0.668	1.73
Moderate or severe liver disease (%)	0.29	0.28	0.957	0.18	0.25	0.25	1.000	0.00	0.25	0.33	0.705	1.53
Metastatic solid tumor (%)	0.08	0.14	0.595	1.71	0.08	0.17	0.564	2.35	0.16	0.16	1.000	0.00
Chronic disease score	1.77 (0.79)	1.73 (0.84)	0.139	4.87	1.74 (0.74)	1.74 (0.85)	0.989	0.05	1.77 (0.80)	1.75 (0.84)	0.574	2.28
Hypertension (%)	11.5	10.1	0.180	4.49	10.1	10.3	0.893	0.54	9.9	10.2	0.840	0.82
Anxiety (%)	11.5	10.1	0.180	11.11	8.0	7.6	0.703	1.55	7.3	7.6	0.758	1.25
Substance abuse (%)	6.7	9.8	0.001	10.02	4.7	4.5	0.771	1.19	4.0	4.7	0.427	3.22
Posttraumatic stress disorder (%)	3.5	5.6	0.002	4.69	1.1	0.9	0.682	1.67	1.1	0.8	0.530	2.54
Headache and migraine (%)	7.3	6.8	0.144	1.80	6.1	6.7	0.505	2.71	6.8	6.8	1.000	0.00
Prior Hospitalization (%)	8.9	4.8	<0.001	16.26	6.9	7.1	0.873	0.65	6.5	7.0	0.628	1.96
Number of unique medication in pre-index period	3.5 (3.5)	3.3 (3.6)	0.001	4.21	3.3 (3.2)	3.3 (3.6)	0.886	0.58	3.4 (3.4)	3.4 (3.6)	0.945	0.82
Use of any psychotropic agent (%)	19.4	22.7	0.016	7.96	22.1	20.9	0.457	3.03	22.2	21.7	0.732	1.39
Average copayment for primary care visit	7.7 (7.8)	7.5 (7.7)	0.438	2.56	7.5 (8.1)	7.6 (8.0)	0.716	1.48	7.3 (8.0)	7.7 (8.0)	0.185	5.37
Quarter of year of treatment initiation												
Quarter 1 (%)	17.9	19.5	0.215	4.10	20.4	18.9	0.356	3.77	18.4	19.2	0.604	2.10
Quarter 2 (%)	19.0	19.1	0.945	0.23	19.5	19.9	0.798	1.04	19.4	20.3	0.612	2.06
Quarter 3 (%)	29.9	31.8	0.214	4.12	31.6	31.3	0.861	0.12	31.6	31.0	0.760	1.23
Quarter 4 (%)	33.2	29.6	0.020	7.74	28.5	29.9	0.446	3.10	30.6	29.5	0.566	2.32

Matching yielded more balanced groups as indicated by smaller standardized differences. All the observed variables had no significant differences between groups after matching. In addition, greedy matching provider better balance with smaller standardized differences compared to Mahalanobis matching with calipers. Therefore, greedy matching was chosen to be used as the matching strategy of the propensity score analysis in this dissertation. Results for Aims 2 and Aim 3 were compared before and after matching.

Key characteristics were compared between individuals who were matched and un-matched (Table 3.13). As expected, they differed in the characteristics that strongly predict the likelihood of provider choice in Table 3.10 and resulted in difficulties in finding matches. Patients initially prescribed an antidepressant by PCPs but were unable to be matched with similar patients initially prescribed an antidepressant by psychiatrist were more likely to be older, female, without prior mental health and non-mental health specialty care, without prior psychotherapy, without prior use of psychotropic agent, without pre-existing anxiety and substance abuse, and had a higher Chronic Disease Score compared with patients initially prescribed an antidepressant by PCPs who were matched. Patients initially prescribed an antidepressant by psychiatrists but were unable to be matched with similar patients initially prescribed an antidepressant by PCPs were more likely to be younger, male, had prior mental health and non-mental health specialty care, prior psychotherapy, use of psychotropic agents, and had pre-existing anxiety and substance abuse compared with patients initially prescribed by psychiatrists who were matched. The comparison shows that individuals who were left out had a much higher or lower propensity score because it is difficult to find a match. It highlights the limitation that the findings found based on the matched cohort might not be generalized to those who were discarded.

Table 3.13 Characteristics between Matched and Un-matched Individuals

	PCP			PSY		
	Matched	Unmatched	P-value	Matched	Unmatched	P-value
Number of observations	1,204	1,237		1,204	239	
Age	39.0	42.9	<0.001	38.2	32.7	<0.001
Male (%)	39.3	21.8	<0.001	40.5	51.1	0.002
Use of mental health-related specialty care during pre-index period (%)	16.9	1.1	<0.001	17.2	74.9	<0.001
Use of non-mental health-related specialty care during pre-index period (%)	33.3	23.2	<0.001	33.1	43.9	0.001
Prior psychotherapy (%)	12.7	1.1	<0.001	12.3	49.4	<0.001
Chronic disease score	1.7	1.8	0.028	1.73	1.71	0.702
Anxiety (%)	8.0	5.5	0.015	7.6	20.9	<0.001
Substance abuse (%)	4.7	2.3	0.001	4.5	11.3	<0.001
Prior Hospitalization (%)	6.9	2.8	<0.001	7.1	18.4	<0.001
Use of any psychotropic agent (%)	22.1	16.8	0.001	20.8	31.8	<0.001
Average copay for primary care visit	7.5	7.9	0.191	7.6	6.9	0.232

All analyses in Aim 2 and 3 have been performed with original sample and propensity score matched sample. If there are no unobservable confounders and effect modification, the propensity score method should produce similar results with overlapping confidence intervals when the confounders are also correctly adjusted in the regression models.

3.7.2 Unobservable Confounding

Confounding is a scenario of mixing effects of exposure with that of a third factor. Confounding will distort the apparent effect of an exposure brought about by the association with other factors that can influence the outcome. A confounder must be associated with both outcome and exposure, but not be part of the causal pathway. Bias results from omitted variables which is a confounder of exposure and outcome.

One of the relationships particularly subject to unobservable confounding in this dissertation is between receipt of guideline-concordant follow-up visits and acute phase completion. These two outcomes were measured in the same time period; hence, it is plausible that there are common omitted variables influencing both of them. In other words, the error terms of these two equations might be correlated. Initial efforts have been made to identify an instrument for follow-up visits in this dissertation.[114] After exploration of internal and external data sources, all the hypothesized instruments, including primary care visit copayment and number of psychiatrist per 10,000 of the residing state, were insignificant or weak instruments based on the F-test.

3.8 Summary

This dissertation utilized a retrospective cohort design with claims data. Initial prescriber specialty was obtained from the index antidepressant prescription which we considered a reliable source since the provider who wrote the prescription is most likely the provider who educate and manage the antidepressant therapy. Guideline-concordant follow-up visits, acute phase and continuation phase antidepressant treatment completion, and subsequent healthcare utilization were extracted based on medical service claims, prescription claims, and facility claims, respectively. Logistic regressions were run to examine the specific aims. In addition, sensitivity analyses were conducted to understand how results may differ by varying the approaches to identify follow-up visits. Finally, propensity score matching was used to achieve balance between patients initially prescribed an antidepressant by PCPs and patients initially prescribed an antidepressant by psychiatrists to adjust for confounding.

CHAPTER IV

RESULTS

This chapter presents the results of this dissertation. Section 4.1 first describes the overall study population, and then follows the results of each aim (section 4.2-4.4).

4.1 Baseline Characteristics of the Study Cohort

This study cohort includes 4,102 patients with MDD who initiated antidepressant treatment. (Table 4.1) They are commercially insured working adults and their dependents (mean age=40). Women account for a larger proportion (65.3%) of the sample likely because depression is more prevalent among women.[1] The majority (85.7%) of the study cohort came from the south and midwest regions of the United States. The median household income of the state of residence averaged $41,600, and the proportion of population with high school education based on the state of residence averaged 80.5%. Forty-one percent of the sample received specialty care during the 6-month period prior to index diagnosis of MDD. The mean Chronic Disease Score (CDS) was 1.77 (min=0.16; max=7.5). 7.7 percent of the study cohort had a diagnosis of anxiety, 4.3% had a diagnosis of alcohol or substance abuse, and 6.7% were hospitalized in the 6-month pre-index period. A small proportion of the cohort had an initial prescriber who was paid on capitated basis (1.5%). The mean out-of-pocket copayment of a 30-day-supply of the initial antidepressant prescription was $13, and the majority of patients (65.8%) were required to pay more than $15. The mean copayment for a primary care provider visit was $7.6. Forty-four percent of patients saw their primary care provider without copayment, while the rest paid a copayment in the $10-$20 range (46%). The majority of patients received an SSRI as initial antidepressant (76.6%). The majority of patients (98.7%) started on a once-daily antidepressant regimen. More patients (62.5%) initiated the antidepressant treatment during the last two quarters of the year (June-December) likely due to the enrollment eligibility window of the study.

Table 4.1 Baseline Characteristics of Study Population

	Number of observations		4,102
	Initial prescriber specialty (%)	Primary Care Provider	59.5
		Psychiatrist	35.2
		Other specialist	5.3
Predisposing	Age (mean, S.D.)		40.0 (12.0)
	Male (%)		34.7
	Region (%)	East North Central	27.7
		East South Central	4.4
		Middle Atlantic	2.0
		Mountain	5.8
		New England	3.5
		Pacific	3.0
		South Atlantic	30.8
		West North Central	12.5
		West South Central	10.3
Enabling	Median household income in state of residence		41,600 (3,919)
	Percent of population with high school education in state of residence		80.5 (3.1)
	Any use of specialty care during pre-index period (%)		41.0
Need	Chronic disease score		1.77 (0.82)
	Anxiety (%)		7.7
	Substance abuse (%)		4.3
	Prior Hospitalization (%)		6.7
Health Plan	Capitated initial prescriber (%)		1.5
	30-day copayment for index antidepressant		18.7 (10.9)
	30-day copayment categories for index antidepressant (%)	$0-$10	12.9
		$10-$15	21.3
		$16-$20	28.6
		>$20	37.2
	Copayment for primary care visit		7.6 (7.9)
	Copayment category for primary care visit (%)	$0	44.0
		$1-$20	50.9
		>$20	5.2
Therapy	Initial antidepressant	Bupropion	10.7
		Citalopram	20.9
		Escitalopram	2.3
		Fluoxetine	12.9
		Mirtazapine	2.8
		Paroxetine	17.0
		Sertraline	23.5
		Venlafaxine	10.0
	Pills for daily doses of initial antidepressant (%)	1	98.7
		≥2	1.3
	Quarter of year of treatment initiation (%)	Quarter 1	18.5
		Quarter 2	19.0
		Quarter 3	30.8
		Quarter 4	31.7

4.2 Aim 1

To examine characteristics among patients initially prescribed an antidepressant by providers with different specialties to treat major depressive disorder (MDD)

4.2.1 Descriptive Analysis

Aim 1 examines characteristics among patients initially prescribed an antidepressant by providers with different specialties to treat MDD. Table 4.2 summarizes the descriptive results of Aim 1, stratified by initial prescriber specialty. 59.5 percent of patients received their initial antidepressant prescription from a primary care provider (PCP), 35.2% from a psychiatrist, and 5.3% from a non-psychiatric specialist. Patients initially prescribed an antidepressant by psychiatrists are more likely to be younger (38.1) compared to patients initially prescribed an antidepressant by PCPs (41.0) or by non-psychiatric specialist (41.1) ($p<0.001$). Patients initially prescribed an antidepressant by psychiatrists are more likely to be male (42.2%) compared to patients initially prescribed an antidepressant by PCPs (30.4%) or by non-psychiatric specialist (33.9%) ($p<0.001$). Patients initially prescribed an antidepressant by psychiatrists (51.1%) or by non-psychiatric specialists (49.5%) are more likely to utilized specialty care in the pre-index period compared to patients initially prescribed an antidepressant by PCPs (34.2%) ($p<0.001$). Patients initially prescribed an antidepressant by non-psychiatric specialists had a significantly higher CDS (1.95, $p<0,001$), while no differences were found between patients initially prescribed an antidepressant by PCPs (1.77) and by psychiatrists (1.73). Patients initially prescribed an antidepressant by psychiatrists were more likely to have pre-existing anxiety (9.8% vs. 6.7%, $p=0.001$) and pre-existing substance abuse (5.6% vs. 3.5%, $p=0.007$) compared to patients initially prescribed an antidepressant by PCPs.

Table 4.2 Baseline Characteristics by Initial Provider Specialty

	Primary Care Provider	Psychiatrist	Non-psychiatric Specialist	P-value
Number of observations	2,441	1,443	218	
% of sample	59.5	35.2	5.3	
Predisposing				
Age	41.0 (11.8)	38.1 (11.9)*	41.1 (12.8)	<0.001
Age categories (%)				
18-34	30.4	38.5*	31.7	<0.001
35-49	45.8	44.4	42.7	0.543
50-64	21.7	15.5*	23.9	<0.001
≥65	2.1	1.5	1.8	0.409
Male (%)	30.4	42.2*	33.9	<0.001
Region (%)				
East North Central	31.4	21.1*	30.3	<0.001
East South Central	5.1	3.2*	5.1	0.017
Middle Atlantic	1.8	2.5	0.9	0.186
Mountain	6.7	3.6*	9.6	<0.001
New England	3.1	3.7	6.9*	0.012
Pacific	3.3	2.5	2.3	0.286
South Atlantic	26.3	39.4*	24.8	<0.001
West North Central	10.4	16.0*	12.4	<0.001
West South Central	11.9	7.9*	7.8	<0.001
Enabling				
Median household income in state of residence	41,656 (3,911)	41,479 (3,956)	41,773 (3,751)	0.316
Percent of population with high school education in state of residence	80.5 (3.3)	80.4 (2.8)	80.8 (3.4)	0.083
Use of specialty care during pre-index period (%)	34.2	51.1*	49.5*	<0.001
Need				
Chronic disease score (CDS)	1.77 (0.79)	1.73 (0.84)	1.95* (1.00)	<0.001
CDS > 2 (%)	28.4	26.8	38.5*	0.002
CDS >3 (%)	7.7	7.6	11.9*	0.075
Anxiety (%)	6.7	9.8*	5.1	0.001
Substance abuse (%)	3.5	5.6*	5.1	0.007
Health Plan-related				
Copayment for primary care visit	7.7 (7.8)	7.5 (8.0)	7.7 (7.4)	0.726
Copayment category for primary care visit (%)				
$0	42.8	46.0	43.1	0.139
$1-$20	51.9	48.9	53.2	0.145
>$20	5.3	5.1	3.7	0.569

* p<0.05 compared to primary care provider group
Standard deviation in parentheses for continuous variables

4.2.2 Multivariate Regression Analysis

Results from multivariate multinomial logistic regression are presented in Table 4.3. The coefficients are presented as odds ratios of each variable comparing receipt of an initial antidepressant prescription from a psychiatrist (psychiatrist model) and a non-psychiatric specialist (non-psychiatric specialist model). Initial receipt of antidepressant prescription from a PCP was the reference category.

In the psychiatrist model, patients with older age were significantly less likely to have a psychiatrist as their initial prescriber for antidepressant treatment (age group 35-49: OR=0.74, 95% CI=0.63-0.86; age group 50-64: OR=0.50, 95% CI=0.40-0.61; age group ≥65: OR=0.43, 95% CI=0.25-0.76; age group18-34 as reference). Male patients were more likely to have psychiatrists as the initial prescriber (OR=1.77, 95% CI=1.53-2.04). Patients with prior specialty care (OR=2.08, 95% CI=1.80-2.40), pre-existing anxiety (OR=1.37, 95% CI=1.07-1.76), and pre-existing substance abuse (OR=1.47, 95% CI=1.06-2.07) were more likely to have a psychiatrist as the initial prescriber. Finally, patients with a PCP copayment greater than zero were less likely to have a psychiatrist as their initial provider (OR=0.85, 95% CI=0.73-0.97).

In the non-psychiatric specialist model, patients having a higher CDS (OR=1.22, 95% CI=1.04-1.42), or having prior specialty care (OR=1.76, 95% CI=1.32-2.35) were more likely to receive an initial antidepressant prescription from a non-psychiatric specialist.

The Hausman test showed the assumption of independence of irrelevant alternatives (IIA) multinomial logit model was not violated, so that the data could be estimated with this model.

In summary, we found that several pre-disposing, enabling and need variables differ among patients initially prescribed an antidepressant by different types of providers. Our results indicate that patients initially prescribed an antidepressant by psychiatrists appear to be more mentally ill, and patients by non-psychiatric specialists tend to have greater physical sickness compared with patients by PCPs.

Table 4.3Multinominal Logistic Regression for Initial Provider Specialty

Psychiatrist		Odds Ratio	95% CI Interval
Age group	18-34	Reference	
	35-49	0.74	(0.63-0.86)
	50-64	0.50	(0.40-0.61)
	≥65	0.43	(0.25-0.76)
Male		1.77	(1.53-2.04)
Region	East North Central	0.50	(0.39-0.63)
	East South Central	0.37	(0.24-0.56)
	Middle Atlantic	0.91	(0.58-1.44)
	Mountain	0.39	(0.26-0.59)
	New England	0.84	(0.56-1.28)
	Pacific	0.54	(0.34-0.87)
	South Atlantic	Reference	
	West North Central	1.16	(0.87-1.51)
	West South Central	0.40	(0.30-0.53)
Median household income (per 1000)		0.98	(0.95-1.01)
Percent with high school education		0.99	(0.95-1.03)
Prior specialty care		2.08	(1.80-2.40)
Chronic disease score		0.91	(0.83-1.00)
Anxiety		1.37	(1.07-1.76)
Substance abuse		1.47	(1.06-2.07)
Copayment of PCP visits	$0	Reference	
	>$0	0.85	(0.73-0.97)
Non-psychiatric Specialist			
Age group	18-34	Reference	
	35-49	0.83	(0.60-1.16)
	50-64	0.81	(0.54-1.21)
	≥65	0.54	(0.19-1.55)
Male		1.21	(0.90-1.62)
Region	East North Central	1.22	(0.74-2.00)
	East South Central	0.92	(0.43-1.96)
	Middle Atlantic	0.64	(0.15-2.75)
	Mountain	1.82	(0.98-3.38)
	New England	2.78	(1.34-5.73)
	Pacific	1.04	(0.38-2.80)
	South Atlantic	Reference	
	West North Central	1.55	(0.87-2.78)
	West South Central	0.64	(0.34-1.21)
Median household income (per 1000)		0.96	(0.90-1.01)
Percent with high school education		1.01	(0.93-1.09)
Prior specialty care		1.76	(1.32-2.35)
Chronic disease score		1.22	(1.04-1.42)
Anxiety		0.61	(0.32-1.17)
Substance abuse		1.21	(0.64-2.28)
Copayment for PCP visits	$0	Reference	
	>$0	1.01	(0.75-1.34)

4.3 Aim 2

To examine the association of antidepressant treatment with initial prescriber specialty and receipt of guideline-concordant outpatient follow-up visits among patients with MDD

We sought to understand the association between initial prescriber specialty, receipt of guideline-concordant outpatient follow-up visits, and antidepressant treatment among patients with MDD in research Aim 2. We first present the results investigating how initial prescriber specialty and other factors might affect receipt of guideline-concordant follow-up visits in section 4.3.1. Next, findings with antidepressant treatment completion as the dependent variable are presented in section 4.3.2.

4.3.1 Follow-up Analysis

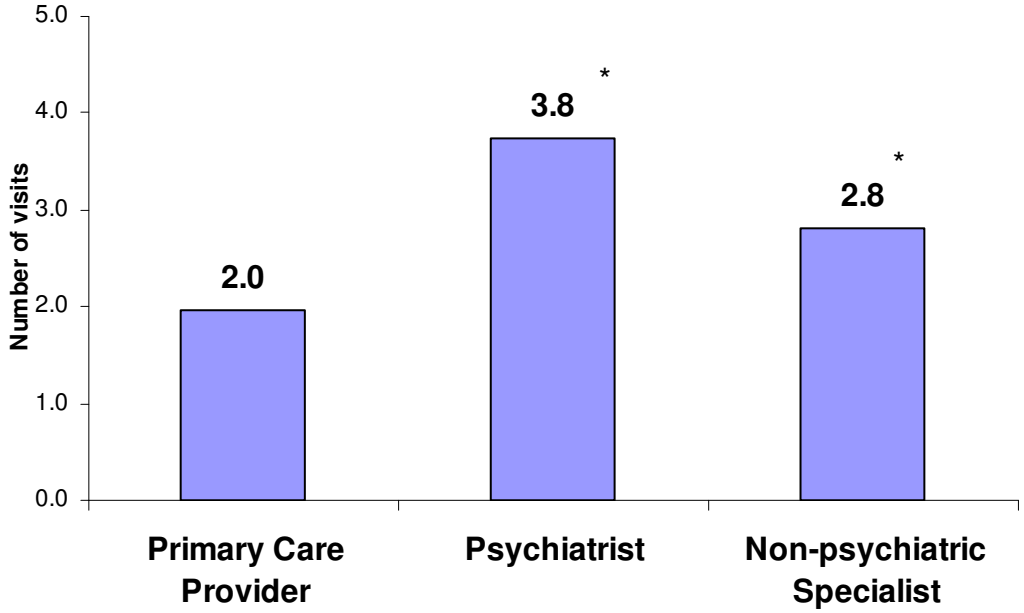
H2.1: Receipt of guideline-concordant outpatient follow-up visits varies by initial prescriber specialty

4.3.1.1 Descriptive Analyses

The mean number of follow-up visits in the entire sample of 4,102 patients was 2.64. When stratified by provider specialty, patients initially prescribed an antidepressant by a psychiatrist had a statistically significantly higher mean number of visits (3.8) compared with patients initially prescribed an antidepressant by a non-psychiatric specialist (2.8) or a PCP (2.0) ($p<0.05$) (Figure 4.1). The proportion of patients who received guideline-concordant follow-up visits, defined by having at least three mental health-related visits and at least one visit made to a provider with prescribing privileges during the 90 days since index antidepressant prescription based on HEDIS measures, was the highest for the psychiatrists

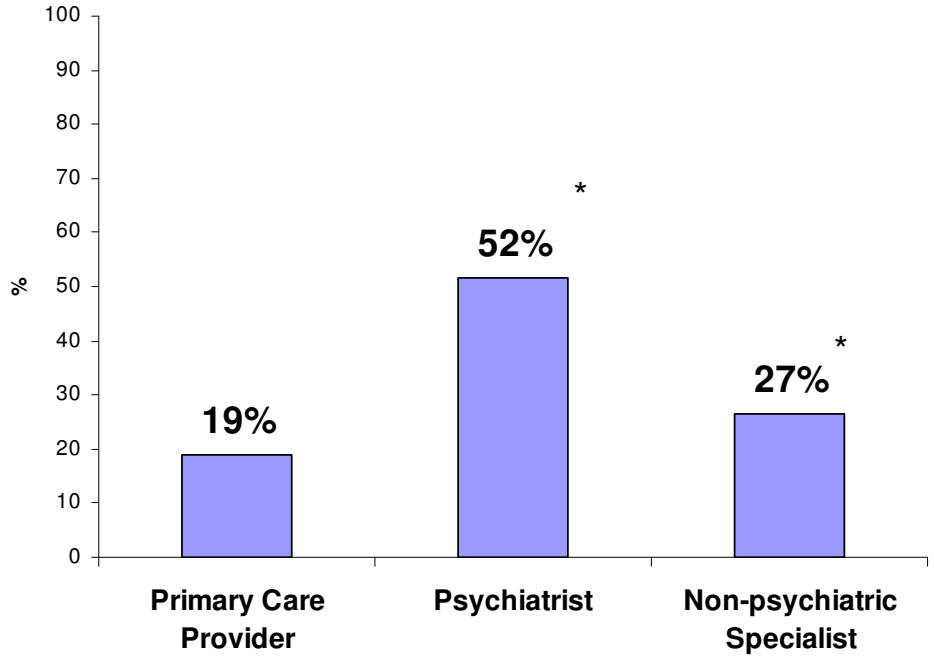
group (52%), followed by other specialists group (27%) and PCP group (19%) ($p<0.05$) (Figure 4.2).

Figure 4.1 Mean Number of Follow-up Visits by Initial Prescriber Specialty



*p<0.05 compared to PCP

Figure 4.2 Proportion of Patient Who Received Guideline-concordant Follow-up Visits by Initial Prescriber Specialty



*p<0.05 compared to PCP

Table 4.4 presents the descriptive results for Aim 2 that compares patients who received guideline-concordant follow-up visits with patients who did not. Thirty-one percent of overall cohort received guideline-concordant follow-up visits. A statistically significantly lower proportion of patients who had guideline-concordant follow-up visits received their initial prescription from a PCP (37%) than patients who did not have guideline-concordant follow-up visits (70%) ($p<0.001$). A statistically significantly higher proportion of patients who had guideline-concordant follow-up visits received their initial prescription from a psychiatrist (59%) than patients who did not have guideline-concordant follow-up visits (25%) ($p<0.001$). Patients who received guideline-concordant follow-up visits were statistically significantly younger (38.8) than patients who did not receive guideline-concordant follow-up visits (40.5) ($p<0.001$). Patients who received guideline-concordant follow-up visits were more likely to be male (39% vs. 33%, $p<0.001$), resided in states with a higher median household income ($41,926 vs. $41,454, $p<0.001$) and in states with a higher proportion of population with high school education (80.7% vs. 80.4%, $p=0.002$) than patients who did not receive guideline-concordant follow-up visits. The CDS was similar between groups, but the guideline-concordant group appeared to have more mental health needs with a statistically significantly higher proportion of patients having pre-existing anxiety (11.2% vs. 6.1%, $p<0.001$) and substance abuse (5.6% vs. 3.8%, $p=0.008$) compared with non-guideline-concordant group. A higher proportion of patients who did not receive guideline-concordant follow-up visits were in the highest PCP copayment group (>$20) than patients who received guideline-concordant follow-up visits (5.8% vs. 3.8%, $p=0.008$).

Table 4.4 Baseline Characteristics between Patients who Received Guideline-concordant Follow-up Visits and Patients Who Did Not

	Receipt of Guideline-concordant Follow-up	No Receipt of Guideline-concordant Follow-up	P-value
Number of observations	1,265	2,837	
% of sample	30.8	69.2	
Primary care provider (%)	36.7	69.7	<0.001
Psychiatrist (%)	58.7	24.7	<0.001
Non-psychiatric specialist (%)	4.6	5.6	0.164
Age	38.8 (11.4)	40.5 (12.2)	<0.001
Age categories (%)			
18-34	35.5	32.4	0.052
35-49	47.4	44.1	0.056
50-64	16.4	21.1	<0.001
≥65	0.8	2.4	0.001
Male (%)	39.1	32.8	<0.001
Region (%)			
East North Central	29.2	27.1	0.173
East South Central	2.9	5.2	0.001
Middle Atlantic	2.4	1.9	0.290
Mountain	4.3	6.4	0.006
New England	5.8	2.5	<0.001
Pacific	2.9	3.0	0.747
South Atlantic	32.7	30.0	0.089
West North Central	12.4	12.5	0.952
West South Central	7.7	11.5	<0.001
Median income in state of residence	41,926 (3,869)	41,454 (3,933)	<0.001
% high school education in state of residence	80.7 (2.9)	80.4 (3.2)	0.002
Chronic disease score	1.77 (0.83)	1.77 (0.82)	0.930
Anxiety (%)	11.2	6.1	<0.001
Substance abuse (%)	5.6	3.8	0.008
Pregnancy-related visits during acute phase (%)	0.3	0.7	0.132
Capitated initial prescriber (%)	1.4	1.5	0.821
Copayment for PCP visits	7.4 (7.6)	7.8 (8.0)	0.139
Copayment category for PCP visit (%)			
$0	44.0	43.9	0.930
$1-$10	5.3	4.8	0.462
$11-$20	46.9	45.6	0.440
>$20	3.8	5.8	0.008
Initial antidepressant (%)			
Bupropion	9.4	11.2	0.084
Citalopram	20.6	21.0	0.721
Escitalopram	2.6	2.2	0.448
Fluoxetine	12.3	13.2	0.453
Mirtazapine	3.6	2.5	0.051
Paroxetine	16.7	17.1	0.743
Sertraline	23.8	23.3	0.748
Venlafaxine	11.1	9.5	0.109
Received psychotherapy in acute phase (%)	79.4	18.2	<0.001
Quarter of year of treatment initiation (%)			
Quarter 1	18.3	18.6	0.790
Quarter 2	18.5	19.2	0.591
Quarter 3	32.7	30.0	0.085
Quarter 4	30.6	32.2	0.302

4.3.1.2 Multivariate Regression Analysis

Results from the logistic regression examining receipt of guideline-concordant follow-up visits are presented in Table 4.5. We found that patients initially prescribed an antidepressant by psychiatrists statistically significantly more likely to receive guideline-concordant follow-up visits than patients initially prescribed an antidepressant by PCPs (OR=4.60, 95% CI =3.94-5.37). Initial antidepressant prescription from non-psychiatric specialists was also significant (OR=1.46, 95% CI =1.06-2.01). Patients aged 50-64 years old (OR=0.77, 95% CI = 0.62-0.96) and greater than 65 years old (OR=0.26, 95% CI=0.12-0.57) were statistically significantly less likely to receive guideline-concordant follow-up visits compared with patients aged 18-34 years old. Patients paying more than $20 for a PCP visit were less likely to receive guideline-concordant follow-up visits (OR=0.63, 95% CI=0.44-0.90) compared with patients paying zero copayment. Finally, patients with pre-existing anxiety were more likely to receive guideline-concordant-follow-up visits. (OR=1.79, 95% CI=1.37-2.32)

Table 4.5 Logistic Regression for Receipt of Guideline-concordant Follow-up Visits

Variable	Category	Odds Ratio	95% CI
Primary care provider		Reference	
Psychiatrist		4.60	(3.94-5.37)
Non-psychiatric specialist		1.46	(1.06-2.01)
Age group	18-34	Reference	
	35-49	1.04	(0.87-1.23)
	50-64	0.77	(0.62-0.96)
	≥65	0.26	(0.12-0.57)
Male		1.12	(0.96-1.31)
Region	East North Central	1.13	(0.87-1.46)
	East South Central	0.78	(0.50-1.24)
	Middle Atlantic	1.06	(0.65-1.72)
	Mountain	0.69	(0.46-1.05)
	New England	2.27	(1.48-3.49)
	Pacific	0.96	(0.57-1.62)
	South Atlantic	Reference	
	West North Central	0.77	(0.57-1.04)
	West South Central	0.94	(0.68-1.29)
Median income (per 1000) in state of residence		1.02	(0.99-1.05)
Percent with high school education in state of residence		1.03	(0.98-1.08)
Pregnancy-related visits during acute phase		0.32	(0.09-1.11)
Chronic disease score		1.05	(0.96-1.15)
Anxiety		1.79	(1.37-2.32)
Substance abuse		1.27	(0.91-1.77)
Capitated initial prescriber		0.87	(0.47-1.63)
Copayment for PCP	$0	Reference	
	$1-$20	1.03	(0.89-1.20)
	>$20	0.63	(0.44-0.90)
Initial antidepressant	Bupropion	0.83	(0.62-1.12)
	Citalopram	1.04	(0.81-1.35)
	Escitalopram	1.07	(0.64-1.81)
	Fluoxetine	Reference	
	Mirtazapine	0.90	(0.56-1.45)
	Paroxetine	1.08	(0.83-1.41)
	Sertraline	1.08	(0.84-1.38)
	Venlafaxine	1.21	(0.90-1.63)
Quarter of year	Quarter 1	Reference	
	Quarter 2	1.05	(0.83-1.33)
	Quarter 3	1.17	(0.95-1.44)
	Quarter 4	1.06	(0.86-1.31)

Sample size = 4,102
C-statistic = 0.72

4.3.1.3 Sensitivity Analyses

Table 4.6 reports results of two sensitivity analyses that varied the approaches to identify follow-up visits. We limited the visits coded with mental health diagnosis only to those made to providers with prescribing privileges in the first sensitivity analysis because these providers, such as psychologists or social workers, can not change patient's antidepressant regimen. We found a large reduction in mean number of visits from 2.6 to 1.4, and the proportion that met the criteria with three or more visits during acute phase dropped from 31% to 18%. In the regression model with this outcome specification, the odds ratios for provider specialty were similar.

We added the visits made to the same provider who wrote the initial antidepressant prescription to the visits in the first sensitivity analysis as the outcome in the second sensitivity analysis. These additional visits, even though there might not be a mental health diagnosis coded on the claim, were made to the initial prescriber and provided opportunities for patients to discuss their antidepressant therapy. We also found a decrease in mean number of visits from 2.6 to 1.9, and the proportion that met the criteria with three or more visits during acute phase dropped from 31% to 27%. In the logistic regression, we found the odds ratio for psychiatrist became much smaller but still significant (OR=2.28, 95% CI=1.95-2.66). The odds ratio for other specialist became insignificant (OR=1.19, 95% CI=0.85-1.67).

4.3.1.4 Propensity Score Matching

Table 4.6 also presents the results from propensity score matching for main and sensitivity analyses. The odds ratio for psychiatrist in the main regression model became smaller in magnitude after the matching (OR=3.87, 95% CI=3.21-4.66), but remained significant after propensity score matching. However, the confidence intervals overlapped, so

there is little difference in results of the original model and propensity score model. The odds ratios for the two sensitivity analyses remained similar after the propensity score matching (Table 4.6). The confidence intervals of the odds ratios overlapped before and after matching.

Table 4.6 Results from Sensitivity Analyses by Varying Approaches to Identify Follow-up Visits and Propensity Score Matching

	Main analysis	Sensitivity #1	Sensitivity #2
Mean number of visits[§]	2.64 (3.01)	1.44 (1.61)	1.93 (2.14)
Receipt three or more visits	30.8%	18.0%	26.7%
	Odds ratios from Pre-matching Logistic Regression[δ]		
Sample size		N=4,102	
Primary care provider	Reference	Reference	Reference
Psychiatrist	4.60* (3.94-5.37)	4.43* (3.69-5.33)	2.28* (1.95-2.66)
Non-psychiatric specialist	1.46* (1.06-2.01)	1.64* (1.11-2.44)	1.19 (0.85-1.67)
	Odds ratios from Post-matching Logistic Regression[δ]		
Sample size		N=2,408	
Primary care provider	Reference	Reference	Reference
Psychiatrist	3.87* (3.21-4.66)	4.32* (3.42-5.45)	2.35* (1.94-2.85)
Non-psychiatric specialist	-	-	-

Note: 95% CI in parentheses. Main analyses used HEDIS measure. Sensitivity analysis #1 restricted visits to only those made to providers with prescribing privileges. Sensitivity analysis #2 added visits made to the initial prescriber to the visits in sensitivity analysis #1.
[§]Standard deviation in the parentheses for mean number of visits
[δ]Regressions include all the covariates listed in Table 4.5
*p<0.05

In summary, our findings from this aim show that initial prescription from a psychiatrist is the strongest predictor of guideline-concordant follow-up visits after conducting sensitivity analyses to address the issue of potential under-coding of mental health diagnosis.

4.3.2 Antidepressant Analyses

H2.2: Completion of antidepressant acute and continuation phase varies by initial prescriber specialty

This section presents results examining factors associated with acute phase completion (section 4.3.2.1) and continuation phase completion (4.3.2.2). Completion of acute and continuation phase were determined by examination of antidepressant refill records in concordance with guideline recommendations. Whether provider specialty affects antidepressant treatment completion was inconsistent in prior studies. This dissertation evaluates the association controlling for guideline-concordant follow-up visits.

4.3.2.1 Acute Phase

4.3.2.1.1 Descriptive Analyses

Overall, 46.8% of the study cohort completed acute phase. When stratified by initial prescriber specialty, there was no statistically significant difference in rate of completion (Figure 4.3). When further stratified by initial prescriber specialty and receipt of guideline-concordant follow-up visits, there was a significant difference of the follow-up visits within each provider specialty (Figure 4.4). This suggests that an interaction term may be appropriate to include in the regression analysis.

Figure 4.3 Proportion of Patients Completed Acute Phase by Initial Prescriber Specialty

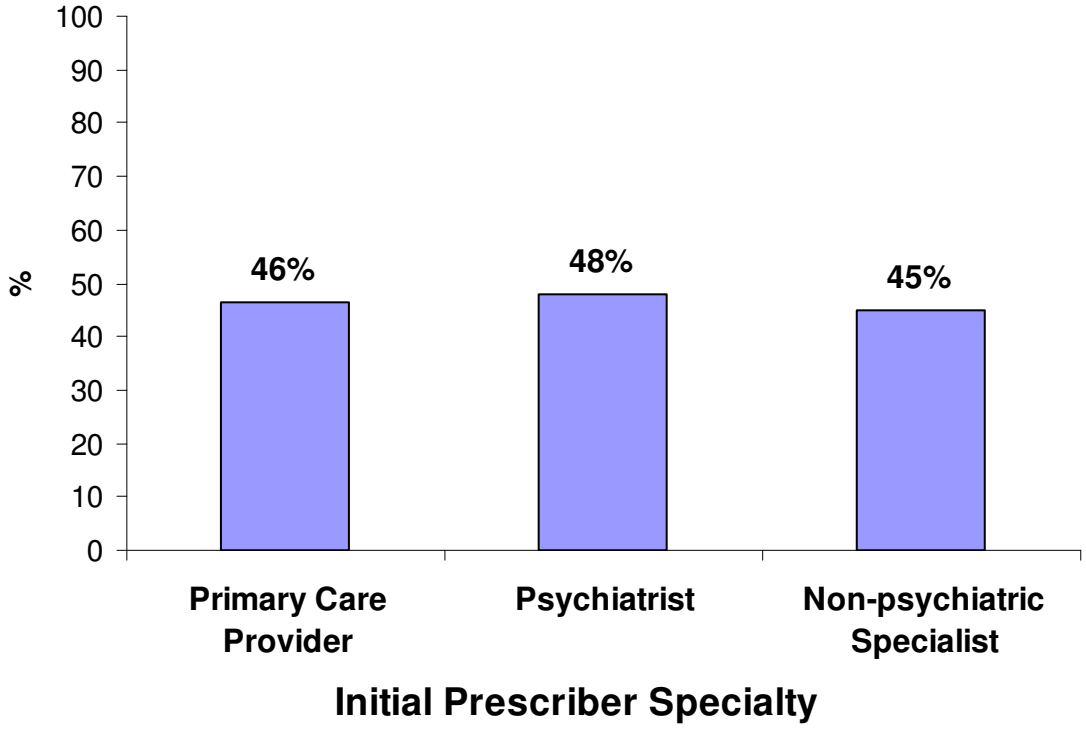
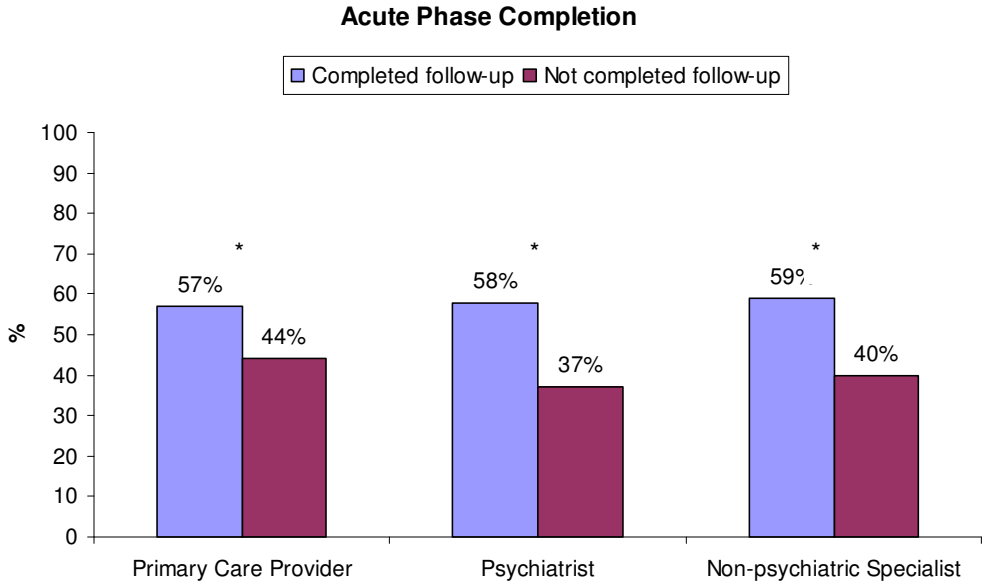


Figure 4.4 Proportion of Patients Completed Acute Phase by Initial Prescriber Specialty and Guideline-concordant Follow-up Visits



* p<0.05 between follow-up completion group within provider specialty

Table 4.7 presents the descriptive results between patients who completed acute phase and patients who did not. Similar to what Figure 4.3 showed, the proportion of patients who received initial antidepressant prescription from different provider specialties was similar across the groups. The proportion of patients who received guideline-concordant follow-up visits was statistically significantly higher among patients who completed acute phase (38.1%) than patients who did not (24.5%) ($p<0.001$). Patients who completed acute phase antidepressant treatment were statistically significantly older (41 vs. 39, $p<0.001$), lived in states with a higher median household income ($41,872 vs. $41,359, $p<0.001$) and in states with higher proportion of population with high school education (80.7% vs. 80.3%, $p<0.001$) than patients who did not complete acute phase. Patients who completed acute phase antidepressant treatment had a higher CDS (1.8 vs. 1.7, $p=0.003$), were less likely to have pre-existing substance abuse (3.5% vs. 5.1%, $p=0.012$), less likely to have pregnancy-related visits during acute phase (0.2% vs. 0.9%, $p=0.003$), and less likely to take a more-than-once-daily antidepressant regimen (0.8% vs. 1.8%, $p=0.003$) compared with patients who completed acute phase.

Table 4.7 Baseline Characteristics between Patients who Completed Acute Phase and Patients Who Did Not

	Completed Acute Phase	Not Completed Acute Phase	P-value
Number of observations	1,921	2,181	
% of sample	46.8	53.2	
Primary care provider (%)	58.8	60.2	0.367
Psychiatrist (%)	36.1	34.3	0.232
Non-psychiatric specialist (%)	5.1	5.5	0.568
Guideline-concordant follow-up visits (%)	38.1	24.5	<0.001
Age	41.0 (12.0)	39.1 (11.9)	<0.001
Age categories			
18-34	29.4	36.8	<0.001
35-49	47.4	43.1	0.005
50-64	20.6	18.8	0.156
≥65	2.6	1.3	0.002
Male (%)	34.2	35.2	0.497
Region (%)			
East North Central	29.7	26.0	0.010
East South Central	3.7	5.1	0.031
Middle Atlantic	2.5	1.6	0.042
Mountain	4.8	6.6	0.013
New England	4.2	2.9	0.033
Pacific	2.9	3.0	0.835
South Atlantic	30.0	31.6	0.280
West North Central	13.4	11.6	0.077
West South Central	8.9	11.6	0.004
Median household income in state of residence	41,872 (3,821)	41,359 (3,988)	<0.001
% with high school education is state of residence	80.7 (3.1)	80.3 (3.1)	<0.001
Chronic disease score	1.81 (0.85)	1.73 (0.80)	0.003
Anxiety (%)	8.5	7.0	0.078
Substance abuse (%)	3.5	5.1	0.012
Pregnancy-related visits during acute phase (%)	0.2	0.9	0.003
30-day copayment for index antidepressant	18.4 (10.0)	18.9 (11.6)	0.084
30-day copayment categories for index antidepressant (%)			
$0-$10	12.6	13.1	0.623
$11-$15	21.2	21.4	0.921
$16-$20	30.0	27.5	0.075
>$20	36.2	38.1	0.215
Initial antidepressant (%)			
Bupropion	8.8	12.3	<0.001
Citalopram	21.5	20.4	0.369
Escitalopram	2.1	2.5	0.413
Fluoxetine	13.5	12.4	0.314
Mirtazapine	1.9	3.6	0.001
Paroxetine	17.2	16.7	0.673
Sertraline	23.9	23.1	0.554
Venlafaxine	11.1	8.9	0.017
More than one pill for daily antidepressant doses (%)	0.8	1.8	0.003
Quarter of year of treatment initiation (%)			
Quarter 1	19.7	17.4	0.058
Quarter 2	19.4	18.6	0.514
Quarter 3	29.8	31.7	0.187
Quarter 4	31.1	32.3	0.409

Standard deviation in parentheses for continuous variables

4.3.2.1.2 Multivariate Regression Analyses

Table 4.8 presents the odds ratios and 95% confidence intervals from the logistic regression model for acute phase antidepressant treatment completion. Since an interaction term between psychiatrist variable and the variable for receipt of guideline-concordant follow-up visits variable was included, the interpretation of the odds ratios is not straight forward because the outcome is binary. In addition, the significance of the interaction term needs to be examined with the marginal effects via the average of the probability method.[99, 100]

The average of the probability based on the data showed that the interaction effect of psychiatrist and guideline-concordant follow-up visits was significant in some of the subjects. The marginal effect was 6.8 percentage points for the interaction term, which means receipt of guideline-concordant follow-up visits increased the probability of acute phase completion by additional 6.8 percentage points if patients were initially prescribed an antidepressant by a psychiatrist. The psychiatrist main effect was -4.6 percentage points, and the marginal effect of guideline-concordant follow-up visits was 13.1 percentage points. Combining the marginal effects all together, patients initially prescribed an antidepressant by a psychiatrist and having guideline-concordant follow-up visits had 15.3 percentage points higher probability of acute phase completion than patients initially prescribed an antidepressant by a PCP and not having guideline-concordant follow-up visits.

Several other covariates were significant in predicting acute phase completion. Similar to prior studies[2, 6, 13, 15, 43], we found older patients had higher odds of acute phase completion than younger patients (age group 35-49: OR=1.38, 95% CI=1.19-1.60; age group 50-64: OR=1.39, 95% CI=1.15-1.68; age group ≥65: OR=2.77, 95% CI=1.67-4.58; age

group 18-34 as reference). Women who might have conceived during acute phase based on pregnancy-related medical visits were less likely to complete their acute phase antidepressant treatment (OR=0.26, 95% CI=0.08-0.80). It appeared that patients who were pregnant tend to terminate the antidepressant treatment although we were not able to distinguish whether that was based on clinical consideration by the provider or patients' own willingness. Patients with a diagnosis of substance abuse (OR=0.62, 95% CI=0.45-0.86) or were on more complex daily antidepressant regimen (OR=0.32, 95% CI=0.17-0.58) were less likely to complete acute phase antidepressant treatment. Patients taking bupropion (OR=0.64, 95% CI=0.49-0.84) and mirtazapine (OR=0.42, 95% CI=0.27-0.65) were less likely to complete acute phase compared with patients taking fluoxetine.

The results based on seemingly unrelated regression using bivariate probit model to account for correlations between error terms of guideline-concordant follow-up visits and acute phase completion regressions found no difference. Hence, we modeled them separately as presented.

Table 4.8 Logistic Regression for Acute Phase Completion Model

Variable	Category	Odds Ratio	95% CI
Primary care provider		Reference	
Psychiatrist		0.82	(0.68-0.99)
Non-psychiatric specialist		0.90	(0.67-1.19)
Receipt of guideline-concordant follow-up		1.73	(1.41-2.11)
Psychiatrist x follow-up interaction		1.34	(0.99-1.79)
Age group	18-34	Reference	
	35-49	1.38	(1.19-1.60)
	50-64	1.39	(1.15-1.68)
	≥65	2.77	(1.67-4.58)
Male		0.94	(0.82-1.08)
Region	East North Central	1.08	(0.86-1.37)
	East South Central	0.95	(0.66-1.38)
	Middle Atlantic	1.44	(0.89-2.34)
	Mountain	0.70	(0.49-1.01)
	New England	1.20	(0.80-1.78)
	Pacific	0.91	(0.60-1.38)
	South Atlantic	Reference	
	West North Central	1.10	(0.84-1.43)
	West South Central	0.95	(0.73-1.25)
Income (in per 1000)		1.02	(0.99-1.04)
% with high school education		1.02	(0.98-1.06)
Pregnancy-related visits during acute phase		0.26	(0.08-0.80)
Chronic disease score		1.07	(0.99-1.16)
Anxiety		1.11	(0.87-1.41)
Substance abuse		0.62	(0.45-0.86)
30-day antidepressant copay	$0-$10	0.88	(0.70-1.10)
	$11-$15	0.97	(0.81-1.16)
	$16-$20	1.09	(0.93-1.29)
	>$20	Reference	
Daily number of pills	1	Reference	
	≥2	0.32	(0.17-0.58)
Initial antidepressant	Bupropion	0.64	(0.49-0.84)
	Citalopram	0.89	(0.71-1.11)
	Escitalopram	0.80	(0.50-1.26)
	Fluoxetine	Reference	
	Mirtazapine	0.42	(0.27-0.65)
	Paroxetine	0.85	(0.67-1.08)
	Sertraline	0.88	(0.71-1.10)
	Venlafaxine	1.21	(0.91-1.60)
Quarter of year	Quarter 1	Reference	
	Quarter 2	0.94	(0.76-1.16)
	Quarter 3	0.83	(0.69-1.00)
	Quarter 4	0.87	(0.72-1.05)

Sample size= 4,102
C-statistic=0.63

4.3.2.1.3 Propensity Score Matching

A similar logistic regression was run based on the cohort of 2,408 propensity score matched subjects with the same independent variables. Table 4.9 presents the odds ratios and marginal effects of several key independent variables before and after the propensity score matching. The psychiatrist coefficient became insignificant after matching, and the interaction effect also diminished. This is most likely due to marginal significance of these variables and decrease in sample size after the matching. The coefficient and marginal effect of receipt of guideline-concordant follow-up visits increased slightly compared to the pre-matching coefficient. However, results are similar because the confidence intervals overlapped.

Table 4.9 Odds Ratios and Marginal Effects of Provider and Follow-up for Acute Phase Model Before and After Propensity Score Matching

Variable	Pre-matching	Post-matching
	N=4,102	N=2,408
	Odds Ratio	
Primary care provider	Reference	Reference
Psychiatrist	0.82* (0.68-0.99)	0.85 (0.69-1.06)
Non-psychiatric specialist	0.90 (0.67-1.19)	-
Receipt of guideline-concordant follow-up	1.73* (1.41-2.11)	1.90* (1.42-2.54)
Psychiatrist x follow-up interaction	1.33 (0.99-1.79)	1.18 (0.81-1.72)
	Marginal Effects	
Primary care provider	Reference	Reference
Psychiatrist	-0.046	-0.036
Receipt of guideline-concordant follow-up	0.131	0.153
Psychiatrist and follow-up interaction	0.068	0.039

Note: 95% CI in parentheses. Regressions include all the covariates listed in Table 4.8
* $p<0.05$

4.3.2.2 Continuation Phase

4.3.2.2.1 Descriptive Analyses

Continuation phase analyses were conducted on the sub-sample who completed acute phase. (N=1,921). Overall, 44.9% of these patients completed continuation phase, and no significant difference was found when stratified by provider specialty (Figure 4.5).

When comparing the difference between patients who completed continuation phase and patients who did not in the descriptive analysis, few variables were significant (Table 4.10). Patients who completed continuation phase antidepressant treatment were more likely to be older (42.5 vs. 39.8, $p<0.001$), to receive three or more outpatient follow-up visits during continuation phase (40.4% vs. 36.1%, $p=0.047$), and had a higher CDS (1.9 vs. 1.7, $p<0.001$), and less likely to be male (31.8% vs. 36.2%, $p=0.044$) than patients who did not complete continuation phase. There were no unadjusted differences by provider specialty.

Figure 4.5 Proportion of Patients Completed Continuation Phase by Initial Prescriber Specialty

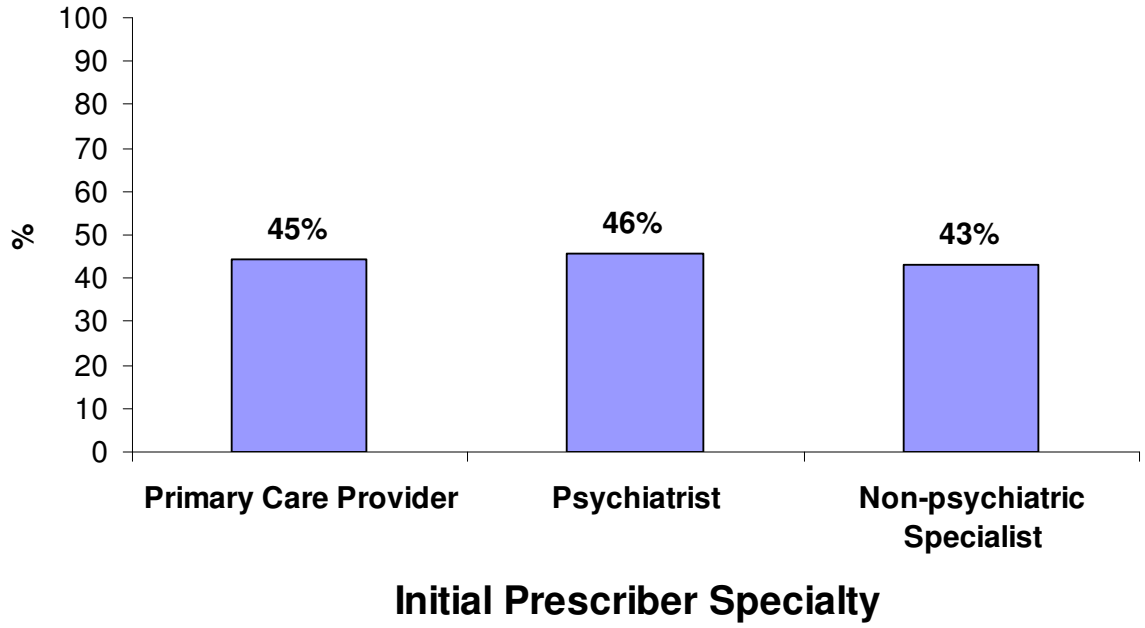


Table 4.10 Baseline Characteristics by Patients who Completed Continuation Phase and Patients Who Did Not

	Completed Continuation Phase	Not Completed Continuation Phase	P-value
Number of observations	862	1,059	
% of sample	44.9	55.1	
Primary care provider (%)	58.4	59.1	0.737
Psychiatrist (%)	36.8	35.6	0.594
Non-psychiatric specialist (%)	4.9	5.3	0.681
≥3 follow-up visits in continuation phase (%)	40.4	36.1	0.047
Age	42.5 (11.8)	39.8 (12.0)	<0.001
Age categories (%)			
18-34	24.7	33.2	<0.001
35-49	48.3	46.7	0.508
50-64	24.3	17.6	<0.001
≥65	2.8	2.5	0.625
Male (%)	31.8	36.2	0.044
Region (%)			
East North Central	29.2	30.0	0.705
East South Central	3.7	3.7	0.973
Middle Atlantic	1.9	3.0	0.104
Mountain	5.3	4.3	0.311
New England	4.3	4.1	0.800
Pacific	2.4	3.3	0.260
South Atlantic	30.6	29.5	0.579
West North Central	14.4	12.7	0.268
West South Central	8.1	9.4	0.310
Median household income in state of residence	41,844 (3,811)	41,896 (3,830)	0.768
% with high school education in state of residence	80.7 (3.1)	80.6 (3.1)	0.702
Chronic disease score	1.88 (0.88)	1.75 (0.82)	<0.001
Anxiety (%)	9.2	7.9	0.335
Substance abuse (%)	3.3	3.7	0.606
Pregnancy-related visits in continuation phase (%)	0.7	1.3	0.179
30-day copayment for index antidepressant	18.3 (9.5)	18.4 (10.4)	0.777
30-day copayment categories for antidepressant (%)			
$0-$10	12.5	12.7	0.935
$11-$15	19.5	22.7	0.091
$16-$20	31.8	28.5	0.120
>$20	36.2	36.2	0.990
Initial antidepressant (%)			
Bupropion	8.4	9.2	0.476
Citalopram	20.8	22.0	0.552
Escitalopram	2.0	2.3	0.657
Fluoxetine	12.3	14.5	0.170
Mirtazapine	2.0	1.8	0.775
Paroxetine	17.89	16.7	0.506
Sertraline	24.5	23.4	0.588
Venlafaxine	12.3	10.2	0.146
More than one pill for daily doses (%)	0.9	0.7	0.508
Quarter of year of treatment initiation (%)			
Quarter 1	19.1	20.2	0.559
Quarter 2	20.9	18.2	0.143
Quarter 3	29.9	29.7	0.894
Quarter 4	30.1	31.9	0.378

Standard deviation in parentheses for continuous variables

4.3.2.2.2 Multivariate Regression Analyses

Table 4.11 presents the odds ratios and 95% confidence intervals from logistic regression for completion of continuation phase antidepressant treatment. Provider specialty was not significant. In this model, we examine receipt of three or more outpatient follow-up visits during the continuation phase and found an OR of 1.59 (95% CI=1.29-1.97). Compared with patients aged 18-34, patients aged 35-49 and aged 50-64 were significantly more likely to complete continuation phase (OR=1.4, 95% CI=1.12-1.74 and OR=1.8, 95% CI=1.36-2.39, respectively). Males were significantly less likely to complete continuation phase (OR=0.79, 95% CI=0.65-0.97).

Table 4.11 Logistic Regression for Continuation Phase Completion Model

Variable	Category	Odds Ratio	95% CI
Primary care provider		Reference	
Psychiatrist		0.99	(0.79-1.21)
Non-psychiatric specialist		0.82	(0.53-1.26)
Received three or more follow-up visits during continuation phase		1.59	(1.29-1.97)
Age group	18-34	Reference	
	35-49	1.40	(1.12-1.74)
	50-64	1.81	(1.36-2.39)
	≥65	1.50	(0.81-2.80)
Male		0.79	(0.65-0.97)
Region	East North Central	1.04	(0.74-1.45)
	East South Central	0.99	(0.55-1.76)
	Middle Atlantic	0.62	(0.33-1.17)
	Mountain	1.44	(0.82-2.53)
	New England	1.09	(0.64-1.87)
	Pacific	0.74	(0.39-1.40)
	South Atlantic	Reference	
	West North Central	1.30	(0.89-1.91)
	West South Central	0.75	(0.50-1.14)
Income (in per 1000)		0.99	(0.96-1.03)
% with high school education		0.98	(0.92-1.04)
Pregnancy-relate visits during continuation phase		0.60	(0.24-1.52)
Chronic disease score		1.13	(1.00-1.27)
Anxiety		1.08	(0.77-1.50)
Substance abuse		0.75	(0.45-1.24)
30-day antidepressant copayment	$0-$10	1.05	(0.76-1.45)
	$11-$15	0.86	(0.66-1.12)
	$16-$20	1.14	(0.90-1.44)
	>$20	Reference	
Daily number of pills	1	Reference	
	≥2	1.15	(0.38-3.48)
Initial antidepressant	Bupropion	1.00	(0.66-1.51)
	Citalopram	1.03	(0.74-1.43)
	Escitalopram	1.10	(0.53-2.27)
	Fluoxetine	Reference	
	Mirtazapine	1.17	(0.59-2.33)
	Paroxetine	1.23	(0.87-1.73)
	Sertraline	1.20	(0.87-1.66)
	Venlafaxine	1.41	(0.95-2.08)
Quarter of year	Quarter 1	Reference	
	Quarter 2	1.25	(0.93-1.68)
	Quarter 3	1.11	(0.85-1.45)
	Quarter 4	1.03	(0.79-1.35)

Sample size=1,921
c-statistic=0.62

4.3.2.2.3 Propensity Score Matching

A logistic regression was run on the sub-sample who completed acute phase based on the propensity score matched sample with the same model specification (N=1,121). Results are generally similar before and after the matching (Table 4.12).

Table 4.12 Odds Ratios of Provider and Follow-up in Continuation Phase Model before and after Propensity Score Matching

Variable	Odds Ratio	
	Pre-matching	Post-matching
	N=1,921	N=1,121
Primary care provider	Reference	Reference
Psychiatrist	0.98 (0.79-1.21)	0.94 (0.72-1.21)
Non-psychiatric specialist	0.82 (0.53-1.26)	-
Received three or more follow-up visits during continuation phase	1.59* (1.29-1.97)	1.86* (1.42-2.44)

Note: 95% CI in parentheses. Regressions include all the covariates listed in Table 4.11
* $p<0.05$

In summary, our analyses shows that receipt of guideline-concordant follow-up visits in the acute phase and receipt of three or more visits during the continuation phase are the strongest predictors in antidepressant treatment completion in each phase respectively, and provider specialty is insignificant.

4.4 Aim 3

To examine the association of subsequent healthcare utilization with initial prescriber specialty and antidepressant treatment among patients with MDD

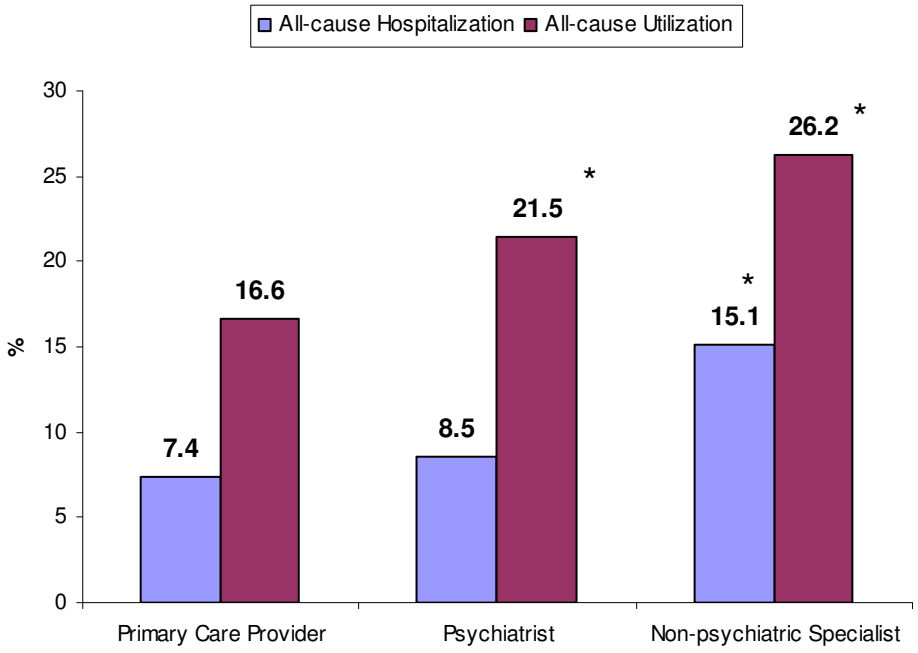
This aim examines whether initial prescriber specialty and antidepressant treatment completion influence healthcare utilization in the subsequent one-year period. The following sections report the results from Aim 3 of acute phase model (4.4.1) and continuation phase models (4.4.2).

4.4.1 Acute Phase

4.4.1.1 Descriptive Analyses

Based on the whole study cohort, we found 18.8% of patients had all-cause utilization (hospitalization or emergency room visits) and 8.2% of patients had all-cause hospitalization during the one-year period after acute phase. When stratified by initial prescriber specialty, a statistically significantly higher proportion of patients initially prescribed an antidepressant by psychiatrists had all-cause utilization (21.5% vs. 16.6%, $p<0.001$), and a statistically significantly higher proportion of patients initially prescribed an antidepressant by non-psychiatric specialists had all-cause utilization (26.2% vs. 16.6%, $p<0.05$) and hospitalization (15.1% vs. 7.4%, $p<0.001$) than patients initially prescribed an antidepressant by PCPs (Figure 4.6).

Figure 4.6 Proportion of All-cause Hospitalization and Utilization by Initial Prescriber Specialty during One-year after Acute Phase



* p<0.05 compared to PCP

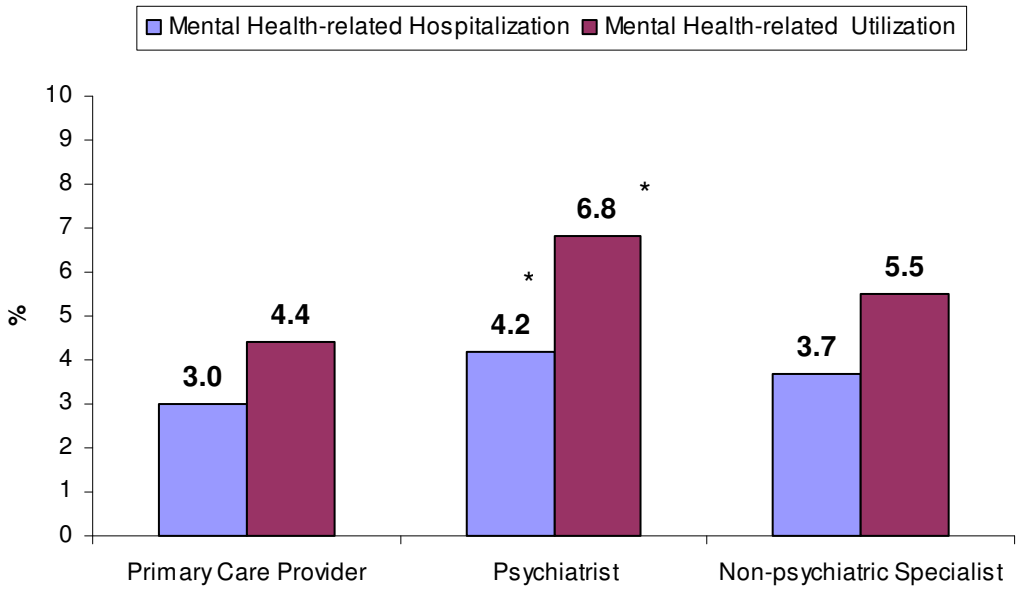
Table 4.13 gives the top ten diagnostic codes of all-cause utilization and hospitalization. The initial utilization, if any, usually was an emergency room visit which was more minor and may or may not lead to a consequent hospital stay. Hence, the distribution of primary diagnosis of these events for all-cause utilization was less concentrated (2.5% for the top ICD-9 code), and more symptom-related (e.g. headache, chest pain, abdominal pain). Mental health-related causes took up two of the top ten Diagnostic Related Group (DRG) in all-cause hospitalization (psychoses and substance abuse). Among the top ten DRG, three of the causes are related to birth delivery (Table 4.13). We did not consider these as adverse events, and we controlled for pregnancy in the statistical models.

Table 4.13 List of Top 10 Primary ICD-9 Diagnosis Codes for All-cause Utilization and Top 10 DRG Codes for All-cause Hospitalization during One Year after Acute Phase

All-cause Utilization				
Rank	ICD-9 code	ICD-9 description	Frequency	Percentage
1	7840	Headache	19	2.46
2	78659	Chest pain	16	2.07
3	34690	Migraine	11	1.42
4	5990	Urinary tract infection	10	1.30
5	78909	Abdominal pain	10	1.30
6	V7612	Screening for malignant neoplasm	10	1.30
7	78650	Chest pain, unspecified	9	1.17
8	8830	Open wound of fingers	9	1.17
9	7242	Lumbogo	8	1.04
10	7802	Syncope and collapse	8	1.04
All-cause Hospitalization				
	DRG code	DRG description	Frequency	Percentage
1	373	Vaginal delivery w/o complicating diagnoses	25	7.44
2	430	Psychoses	23	6.85
3	359	Uterine & Adnexa procedure for non-malignancy w/o complications	16	4.76
4	523	Alcohol/drug abuse or dependent w/o rehabilitation therapy w/o complications	9	2.68
5	288	O.R. procedures for obesity	8	2.38
6	371	Cesarean section w/o complications	8	2.38
7	024	Seizure & headache age>17 with complications	6	1.79
8	358	Uterine & Adnexa procedure for non-malignancy with complications	6	1.79
9	372	Vaginal delivery with complicating diagnoses	6	1.79
10	520	Cervical spinal fusion w/o complications	6	1.79

We found 5.3% of the study cohort had mental health-related utilization (hospital admissions and emergency room visits), and 3.4% of patients had mental health-related hospitalization. When stratified by initial prescriber specialty, a statistically significantly higher proportion of patients initially prescribed an antidepressant by psychiatrists had mental health-related utilization (6.8% vs. 4.4%, $p<0.05$) and mental health-related hospitalization (4.2% vs. 3.0%, $p<0.05$) than patients initially prescribed an antidepressant by PCPs (Figure 4.7).

Figure 4.7 Proportion of Mental Health-related Hospitalization and Utilization by Initial Prescriber Specialty during One-year d after Acute Phase



* $p<0.05$ compared to PCP

Table 4.14 describes the baseline characteristics between patients who had utilization and patients who did not. Patients without all-cause utilization were more likely to complete acute phase antidepressant treatment (47.8% vs. 42.9%, $p=0.015$). Patients with all-cause utilization had statistically significantly lower proportion of male (31.1%) than patients without all-cause utilization (35.6%) ($p<0.001$), which might be confounded by pregnancy. A

statistically significantly higher proportion of patients who had prior hospitalization (12.7% vs. 5.3%, p<0.001), pre-existing substance abuse (6.9% vs. 3.8%, p<0.001), and a higher CDS (2.0 vs. 1.7, p<0.001) were found among patients who had all-cause utilization than patients who did not. Patients who had all-cause utilization were more likely to reside in states with higher median household income ($41,889 vs. $41,532, p=0.023) and in states with a higher proportion of population with high school education (80.8% vs. 80.3%, p<0.001) compared with patients who did not have all-cause utilization.

Among patient with mental health-related utilization, we found a statistically significantly higher proportion of patients initially prescribed by a psychiatrist (45% vs. 35%, p=0.002) and a lower proportion of patients initially prescribed by a PCP (49% vs. 60%, p=0.002) compared with patients without mental health-related utilization. Patients who had mental health-related utilization were more likely to have prior hospitalization (14.3% vs. 6.2%, p<0.001), a higher CDS (2.2 vs. 1.7, p<0.001), pre-existing anxiety (13.4% vs. 7.4 %, p=0.001), and pre-existing substance abuse (13.4% vs. 3.8%, p<0.001) than patients who did not have mental health-related utilization. Patients who had mental health-related utilization were more likely to reside in states with a higher median household income ($42,409 vs. $41,554, p=0.002) and in states with a higher proportion of population with high school education (81.3% vs. 80.4%, p<0.001) compared with patients who did not have mental health-related utilization.

Table 4.15 presents the descriptive results for hospitalization. A statistically significantly lower proportion of patients initially prescribed an antidepressant by a PCP (53.6% vs. 60.0%, p=0.021) and a higher proportion of patients initially prescribed by a non-psychiatric specialist (9.8% vs. 4.9%, p<0.001) were found among patients who had all-cause

hospitalization compared with patients who did not have all-cause hospitalization. Patients who had all-cause hospitalization were more likely to be older (42.1 vs. 39.8, p<0.001), have prior hospitalization (14.9% vs. 5.9%, p<0.001), pregnancy-related visits during acute phase (4.8% vs. 0.2%, p<0.001), a higher CDS (2.3 s. 1.7, p<0.001), pre-existing anxiety (11.6% vs. 7.4%, p=0.005), and pre-existing substance abuse (8.9% vs. 3.9% p<0.001) compared to patients who did not have all-cause hospitalization.

Among patient with mental health-related hospitalization, we found a statistically significantly lower proportion of patients initially prescribed an antidepressant by a PCP (51.4% vs. 59.8%, p=0.048) compared with patients without mental health-related hospitalization. Patients who had mental health-related hospitalization had a statistically significantly higher proportion of patients in ≥65 age groups than patients who did not have mental health-related hospitalization (4.3% vs. 1.8%, p=0.036). Patients who had mental health-related hospitalization were more likely to have prior hospitalization (12.9% vs. 6.4%, p=0.003), pregnancy-related visits during acute phase (2.1% vs. 0.5%, p=0.014), a higher CDS (2.2 vs., 1.8, p<0.001), pre-existing anxiety (16.4% vs. 7.4%, p<0.001), and pre-existing substance abuse (13.6% vs. 4.0%, p<0.001) compared with patients without mental health-related hospitalization. Patients who had mental health-related hospitalization were more likely to reside in states with higher a median household income ($42,746 vs. $41,559 p<0.001) and in states with a higher proportion of population with high school education (81.3% vs. 80.4%, p=0.002) compared with patients without mental health-related hospitalization.

Table 4.14 Baseline Characteristics between Patients Who Had Utilization and Patients Who Did Not for Acute Phase Analysis

	All-cause Utilization			Mental Health-related Utilization		
	Had Utilization	No Utilization	P-value	Had Utilization	No Utilization	P-value
Number of observations	772	3,330		217	3,952	
% of sample	18.8	81.2		5.3	95.7	
Primary care provider (%)	52.5	61.1	0.021	49.3	60.1	0.002
Psychiatrist (%)	40.2	34.0	0.001	45.2	34.6	0.002
Non-psychiatric specialist (%)	7.4	4.8	0.004	5.5	5.3	0.884
Complete acute phase antidepressant treatment (%)	42.9	47.8	0.015	41.9	47.1	0.138
Age	40.0 (12.7)	40.0 (11.8)	0.920	40.9 (12.9)	39.9 (11.9)	0.266
Age categories (%)						
18-34	34.7	33.0	0.372	32.3	33.4	0.726
35-49	42.2	45.8	0.073	41.9	45.3	0.332
50-64	20.7	19.4	0.393	22.6	15.9	0.260
≥65	2.3	1.8	0.331	3.2	1.8	0.142
Male (%)	31.1	35.6	0.018	36.9	34.6	0.499
Median income in state of residence	41,889 (3,769)	41,532 (3,950)	0.023	42,409 (3,861)	41,554 (3,918)	0.002
% population with high school education in state of residence	80.8 (2.9)	80.3 (3.2)	<0.001	81.3 (2.9)	80.4 (3.1)	<0.001
Region (%)						
East North Central	33.9	26.3	<0.001	37.8	27.2	0.001
East South Central	3.6	4.6	0.225	1.8	4.6	0.057
Middle Atlantic	0.8	2.3	0.006	0.5	2.1	0.093
Mountain	4.7	6.0	0.149	5.1	5.8	0.657
New England	4.7	3.2	0.053	5.5	3.4	0.097
Pacific	1.2	3.4	0.001	0.9	3.1	0.067
South Atlantic	29.0	31.2	0.230	26.3	31.1	0.136
West North Central	15.3	11.8	0.008	16.6	12.2	0.058
West South Central	6.9	11.1	0.001	5.5	10.6	0.018
Prior Hospitalization (%)	12.7	5.3	<0.001	14.3	6.2	<0.001
Pregnancy visits during acute phase (%)	2.2	0.2	<0.001	1.4	0.5	0.114
Chronic disease score	2.0 (1.01)	1.7 (0.77)	<0.001	2.2 (1.01)	1.7 (0.81)	<0.001
Anxiety (%)	8.9	7.4	0.153	13.4	7.4	0.001
Substance abuse (%)	6.9	3.8	<0.001	13.4	3.8	<0.001
Quarter of year of treatment initiation (%)						
Quarter 1	20.1	18.1	0.211	21.2	18.4	0.293
Quarter 2	20.6	18.6	0.207	22.6	18.8	0.166
Quarter 3	30.1	31.0	0.622	27.2	31.0	0.238
Quarter 4	29.3	32.3	0.106	29.0	31.9	0.383

Standard deviation in parentheses for continuous variables

Table 4.15 Baseline Characteristics between Patients Who Had Hospitalization and Patients Who Did Not for Acute Phase Analysis

	All-cause Hospitalization			Mental Health-related Hospitalization		
	Hospitalized	Not Hospitalized	P-value	Hospitalized	Not Hospitalized	P-value
Number of observations	336	3,766		140	3,962	
% of sample	8.2	91.8		3.4	96.6	
Primary care provider (%)	53.6	60.0	0.021	51.4	59.8	0.048
Psychiatrist (%)	36.6	35.1	0.567	42.9	34.9	0.053
Non-psychiatric specialist (%)	9.8	4.9	<0.001	5.7	5.3	0.830
Complete acute phase antidepressant treatment (%)	41.1	47.3	0.027	45.7	46.9	0.788
Age	42.1 (13.2)	39.8 (11.9)	<0.001	41.9 (13.3)	39.9 (11.9)	0.054
Age categories						
18-34 (%)	30.4	33.6	0.225	30.7	33.4	0.501
35-49 (%)	40.8	45.5	0.094	39.3	45.3	0.158
50-64 (%)	24.4	19.2	0.021	19.4	25.7	0.065
≥65 (%)	4.5	1.7	<0.001	4.3	1.8	0.036
Male (%)	30.7	35.1	0.101	35.0	34.7	0.947
Median income in state of residence	41,987 (4,151)	41,565 (3,896)	0.058	42,746 (4,049)	41,559 (3,909)	<0.001
% population with high school education in state of residence	80.7 (3.1)	60.4 (3.1)	0.118	81.3 (3.0)	80.4 (3.1)	0.002
East North Central (%)	31.3	27.4	0.134	35.7	27.5	0.032
East South Central (%)	4.2	4.5	0.802	2.1	4.5	0.180
Middle Atlantic (%)	1.8	2.1	0.747	0.7	2.1	0.263
Mountain (%)	6.0	5.7	0.870	5.7	5.7	0.984
New England (%)	4.5	3.4	0.321	5.7	3.4	0.149
Pacific (%)	2.4	3.0	0.504	1.4	3.0	0.273
South Atlantic (%)	26.2	31.2	0.055	23.6	31.1	0.059
West North Central (%)	14.0	12.3	0.375	17.9	12.3	0.049
West South Central (%)	9.8	10.3	0.769	7.1	10.4	0.213
Prior Hospitalization (%)	14.9	5.9	<0.001	12.9	6.4	0.003
Pregnancy visits during acute phase (%)	4.8	0.2	<0.001	2.1	0.5	0.014
Chronic disease score	2.3 (1.16)	1.7 (0.77)	<0.001	2.2 (1.06)	1.8 (0.81)	<0.001
Anxiety (%)	11.6	7.4	0.005	16.4	7.4	<0.001
Substance abuse (%)	8.9	3.9	<0.001	13.6	4.0	<0.001
Quarter of year of treatment initiation						
Quarter 1 (%)	18.8	18.5	0.903	20.0	18.5	0.643
Quarter 2 (%)	19.6	18.9	0.750	24.3	18.8	0.104
Quarter 3 (%)	31.6	30.7	0.753	25.7	31.0	0.186
Quarter 4 (%)	30.1	31.9	0.496	30.0	31.8	0.657

Standard deviation in parentheses for continuous variables

4.4.1.2 Multivariate Regression Analyses

Table 4.16 presents the odds ratios and 95% confidence intervals from acute phase model for utilization. Patients initially prescribed an antidepressant by psychiatrists (OR=1.37, 95% CI=1.15-1.63) and non-psychiatric specialists (OR=1.57, 95% CI=1.12-2.19) were more likely to have all-cause utilization. Patients who completed acute phase were less likely to have all-cause utilization (OR=0.79, 95% CI=0.67-0.93). Men were less likely to have all-cause utilization than women (OR=0.8, 95% CI=0.67-0.95). Patients with pregnancy-related visits during acute phase were much more likely of having all-cause utilization than patients without pregnancy-related visits (OR=8.96, 95%CI=3.38-23.76). Need factors such as prior hospitalization (OR=1.76, 95% CI=1.32-2.35) and higher CDS (OR=1.47, 95% CI=1.33-1.62) appeared to be strong predictors of all-cause utilization.

When limited to mental health-related utilization, only an initial prescription from a psychiatrist was significant (OR=1.54, 95% CI=1.14-2.07). Completion of acute phase antidepressant treatment was marginally significant in preventing mental health-related utilization (OR=0.75, 95% CI=0.56-0.99). A higher CDS (OR=1.52, 95% CI= 1.32-1.75), pre-existing anxiety (OR=1.56, 95% CI=1.04-2.36) and substance abuse (OR=2.87, 95% CI=1.80-4.57) were significant in predicting greater likelihood of mental health-related utilization.

Table 4.17 presents the odds ratios from models for hospitalization. Patients initially prescribed an antidepressant by non-psychiatric specialists were more likely to have all-cause hospitalization (OR=1.99, 95% CI=1.28-3.07) than patients initially prescribed an antidepressant by PCPs. Completion of acute phase antidepressant treatment had a protective effect against risk of all-cause hospitalization (OR=0.75, 95% CI=0.59-0.95). Patients with

pregnancy-related visits during acute phase were much more likely to have all-cause hospitalization (OR=24.6, 95% CI=9.4-64.8). A higher CDS (OR=1.69, 95% CI=1.50-1.90) and pre-existing substance abuse (OR=1.79, 95% CI=1.14-2.82) increased the likelihood of all-cause hospitalization.

When limited to mental health-related hospitalization, neither provider specialty nor completion of acute phase was significant. Only need factors including pregnancy-related visits during acute phase (OR=3.9, 95% CI=1.17-12.95), higher CDS (OR=1.58, 95% CI=1.33-1.88), pre-existing anxiety (OR=2.01, 95% CI=1.26-3.20), and pre-existing substance abuse (OR=3.02, 95% CI=1.76-5.19) were significant.

Table 4.16 Logistic Regressions for Utilization after Acute Phase

		All-cause Utilization		Mental Health-related Utilization	
Variable	Category	Odds Ratio	95% CI	Odds Ratio	95% CI
Primary care provider		Reference		Reference	
Psychiatrist		1.37	(1.15-1.63)	1.54	(1.14-2.07)
Non-psychiatric specialist		1.57	(1.12-2.19)	1.05	(0.55-2.00)
Completed acute phase		0.79	(0.67-0.93)	0.75	(0.56-0.99)
Age group	18-34	Reference		Reference	
	35-49	0.83	(0.69-1.00)	0.85	(0.61-1.19)
	50-64	0.79	(0.62-1.00)	0.87	(0.57-1.32)
	≥65	0.80	(0.44-1.49)	1.13	(0.47-2.73)
Male		0.80	(0.67-0.95)	1.00	(0.74-1.34)
Income (in per 1000)		1.00	(0.96-1.04)	1.02	(0.95-1.09)
% with high school education		0.97	(0.92-1.02)	1.02	(0.93-1.11)
Region	East North Central	1.66	(1.23-2.25)	1.56	(0.92-2.63)
	East South Central	0.79	(0.48-1.30)	0.59	(0.19-1.82)
	Middle Atlantic	0.39	(0.17-0.89)	0.24	(0.03-1.91)
	Mountain	1.03	(0.65-1.65)	1.01	(0.46-2.22)
	New England	1.70	(1.05-2.74)	1.75	(0.76-4.03)
	Pacific	0.41	(0.18-0.86)	0.36	(0.08-1.58)
	South Atlantic	Reference		Reference	
	West North Central	1.60	(1.14-2.24)	1.46	(0.81-1.64)
	West South Central	0.61	(0.42-0.89)	0.77	(0.37-1.58)
Pregnancy visits during acute phase		8.96	(3.38-23.76)	2.14	(0.62-7.40)
Prior Hospitalization		1.76	(1.32-2.35)	1.26	(0.80-1.98)
Chronic disease score		1.47	(1.33-1.62)	1.52	(1.32-1.75)
Anxiety		1.04	(0.77-1.40)	1.56	(1.04-2.36)
Substance abuse		1.40	(0.98-1.99)	2.87	(1.80-4.57)
Quarter of year	Quarter 1	Reference		Reference	
	Quarter 2	1.02	(0.79-1.33)	1.08	(0.71-1.65)
	Quarter 3	0.92	(0.72-1.16)	0.77	(0.51-1.15)
	Quarter 4	0.85	(0.67-1.07)	0.81	(0.54-1.21)
Sample size=4,102	c-statistic=0.66			c-statistic=0.71	

Table 4.17 Logistic Regressions for Hospitalization after Acute Phase

		All-cause Hospitalization		Mental Health-related Hospitalization	
Variable	Category	Odds Ratio	95% CI	Odds Ratio	95% CI
Primary care provider		Reference		Reference	
Psychiatrist		1.17	(0.90-1.51)	1.41	(0.97-2.04)
Non-psychiatric specialist		1.99	(1.28-3.07)	1.09	(0.49-2.41)
Completed acute phase		0.75	(0.59-0.95)	0.87	(0.61-1.25)
Age group	18-34	Reference		Reference	
	35-49	0.92	(0.69-1.22)	0.83	(0.55-1.26)
	50-64	1.02	(0.72-1.45)	1.04	(0.62-1.72)
	≥65	1.59	(0.82-3.10)	1.45	(0.56-3.79)
Male		0.83	(0.64-1.06)	0.93	(0.64-1.35)
Income (in per 1000)		1.05	(0.64-1.06)	1.08	(1.00-1.18)
% with high school education		0.99	(0.91-1.07)	1.00	(0.90-1.11)
Region	East North Central	1.24	(0.80-1.91)	1.31	(0.70-2.45)
	East South Central	1.40	(0.69-2.82)	1.02	(0.27-3.81)
	Middle Atlantic	0.90	(0.38-2.13)	0.32	(0.04-2.64)
	Mountain	1.11	(0.57-2.17)	1.02	(0.40-2.60)
	New England	1.26	(0.62-2.55)	1.41	(0.51-3.94)
	Pacific	0.73	(0.30-1.78)	0.41	(0.08-1.89)
	South Atlantic	Reference		Reference	
	West North Central	1.20	(0.73-1.96)	1.39	(0.70-2.78)
	West South Central	1.30	(0.78-2.19)	1.30	(0.57-2.99)
Pregnancy visits during acute phase		24.63	(9.35-64.83)	3.90	(1.17-12.95)
Prior Hospitalization		1.47	(1.00-2.15)	0.96	(0.54-1.72)
Chronic disease score		1.69	(1.50-1.90)	1.58	(1.33-1.88)
Anxiety		1.36	(0.94-1.97)	2.01	(1.26-3.20)
Substance abuse		1.79	(1.14-2.82)	3.02	(1.76-5.19)
Quarter of year	Quarter 1	Reference		Reference	
	Quarter 2	1.03	(0.71-1.50)	1.28	(0.76-2.14)
	Quarter 3	1.01	(0.72-1.41)	0.78	(0.47-1.31)
	Quarter 4	0.93	(0.66-1.32)	0.90	(0.55-1.48)
Sample size=4,102	c-statistic=0.70			c-statistic=0.72	

4.4.1.3 Propensity Score Matching

Similar logistic regressions were run based on the propensity score matched cohort of 2,408 patients (Table 4.18). The results were generally consistent before and after matching except for the effect of acute phase completion for all-cause and mental health-related utilization model. Completion of acute phase antidepressant treatment had a significant protective effect against all-cause utilization before matching (OR=0.79, 95% CI=0.67-0.93), but such effect became insignificant in the logistic regression model based on the matched cohort (OR=0.86, 95% CI=0.69-1.07). Completion of acute phase antidepressant treatment had a marginally significant protective effect against mental health-related utilization before matching (OR=0.75, 95% CI=0.56-0.99), but such effect became insignificant after the matching (OR=0.79, 95% CI=0.51-1.22).

Table 4.18 Odds Ratios of Utilization and Hospitalization for Acute Phase Model before and after Propensity Score Matching

	Utilization		Hospitalization	
Variable	All-cause	Mental health-related	All-cause	Mental health-related
	Pre-matching			
Sample size	N=4,102			
Primary care provider	Reference	Reference	Reference	Reference
Psychiatrist	1.37* (1.15-1.63)	1.54* (1.14-2.09)	1.17 (0.90-1.51)	1.41 (0.97-2.05)
Non-psychiatric specialist	1.57* (1.12-2.19)	1.05 (0.55-2.00)	1.99* (1.28-3.07)	1.09 (0.49-2.41)
Completed acute phase	0.79* (0.67-0.93)	0.75* (0.56-0.99)	0.75* (0.59-0.95)	0.87 (0.61-1.25)
	Post-matching			
Sample size	N=2,408			
Primary care provider	Reference	Reference	Reference	Reference
Psychiatrist	1.51* (1.22-1.86)	1.67* (1.07-2.61)	1.36 (0.99-1.86)	1.56 (0.99-2.45)
Non-psychiatric specialist	-	-	-	-
Completed acute phase	0.86 (0.70-1.07)	0.79 (0.51-1.22)	0.65* (0.47-0.89)	0.79 (0.49-1.19)

Note: 95% CI in parentheses. Regressions include all the covariates listed in Table 4.16 and Table 4.17
*p<0.05

In summary, we found patients initially prescribed an antidepressant by psychiatrists were statistically significantly more likely to have all-cause and mental health-related

utilization during the one-year period after the acute phase, while patients initially prescribed an antidepressant by non-psychiatric specialists were more likely to have all-cause hospitalization compared with patients initially prescribed by PCPs. We also found that completion of acute phase have a protective effect over all-cause hospitalization.

4.4.2 Continuation Phase

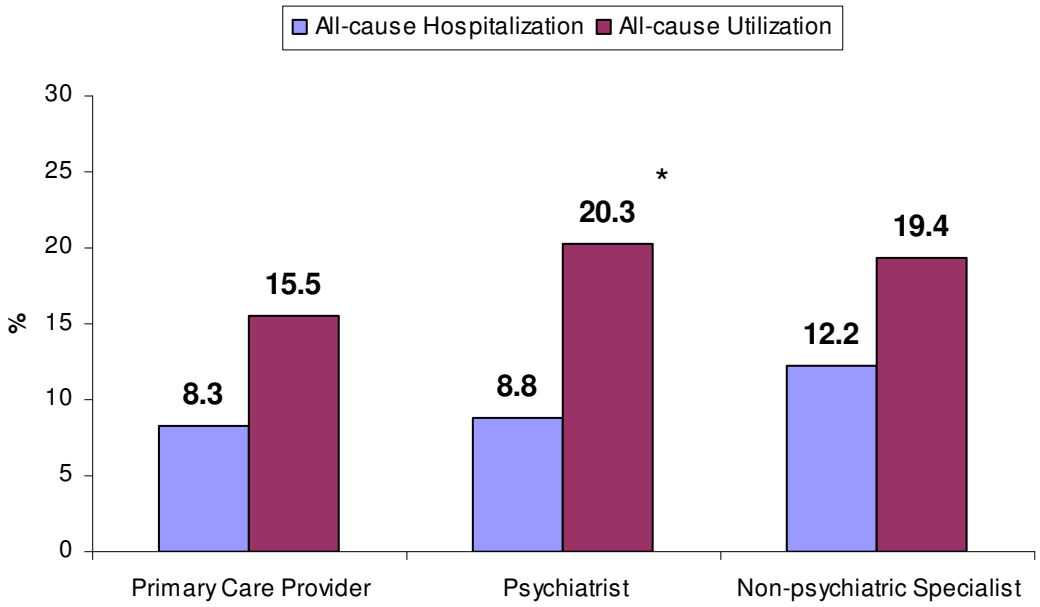
The following section presents the results based on the sub-population of patients who completed acute phase for continuation phase analyses. (N=1,921)

4.4.2.1 Descriptive Analyses

Overall, 17.4% of patients had all-cause utilization (hospitalization or emergency room visits), and 8.7% of patients had hospitalization during the one-year period after the continuation phase antidepressant treatment. When stratified by initial prescriber specialty, a statistically significantly higher proportion of patients initially prescribed an antidepressant by psychiatrists had all-cause utilization (20.3%) than patients initially prescribed an antidepressant by PCPs (15.5%) (p=0.008) (Figure 4.8). Differences were not found between patients initially prescribed an antidepressant by PCPs and by non-psychiatric specialists, which may due to small sample size of the latter group (N=98).

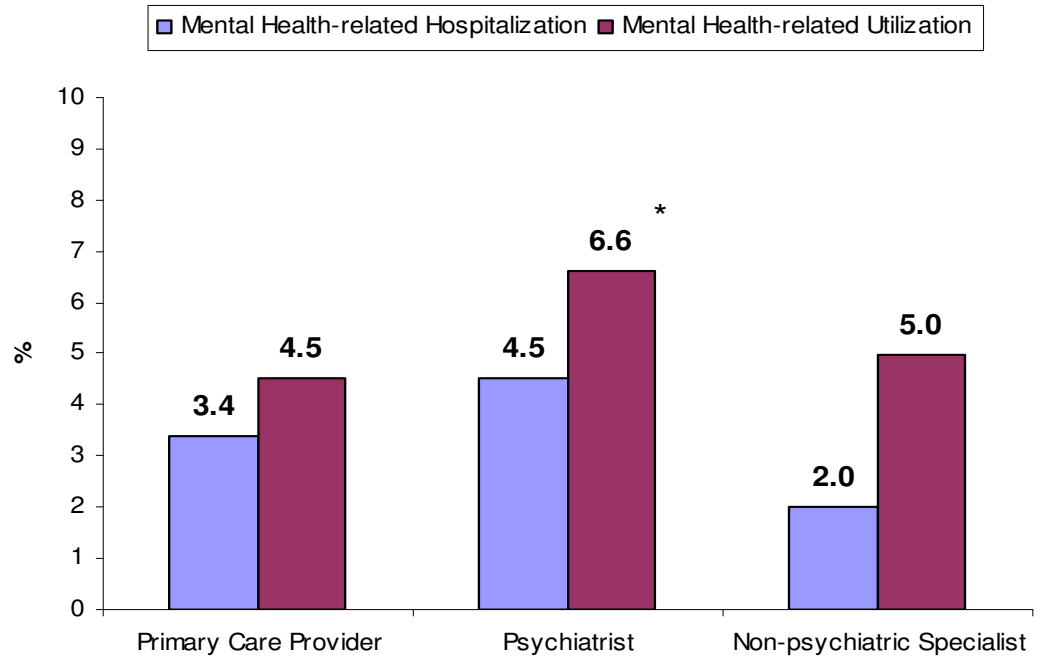
The proportion of patients who had mental health-related utilization and mental health-related hospitalization was 5.3% and 3.7%, respectively. When stratified by initial prescriber specialty, a statistically significantly higher proportion of patients initially prescribed an antidepressant by psychiatrists had all-cause utilization (6.6%) than patients initially prescribed an antidepressant by PCPs (4.5%) ($p<0.05$) (Figure 4.9).

Figure 4.8 Proportion of All-cause Hospitalization and Utilization by Initial Prescriber Specialty during One-year after Continuation Phase



* p<0.05 compared to PCP

Figure 4.9 Proportion of Mental Health-related Hospitalization and Utilization by Initial Prescriber Specialty during One-year after Continuation Phase



* p<0.05 compared to PCP

Table 4.19 presents baseline characteristics between patients who had utilization during the one-year period after the continuation phase and patients who did not. A statistically significantly lower proportion of patients were found to be initially prescribed an antidepressant by a PCP (52.2% vs. 60.1%, p=0.008) and a higher proportion was found to be initially prescribed an antidepressant by a psychiatrist (42.1% vs. 34.9%, p=0.012) among patients who had all-cause utilization than patients who did not have all-cause utilization. Patients who had all-cause utilization were more likely to be older (42.5 vs. 40.6, p=0.008), have prior hospitalization (12.8% vs. 5.1%, p<0.001), have a higher CDS (2.1 vs. 1.7, p<0.001), have pregnancy-related visits during continuation phase (3.9% vs. 0.4%, p<0.001), and have pre-existing substance abuse (11.0% vs. 7.9%, p=0.038) compared with patients who did not have all-cause utilization. Patients who had all-cause utilization were more likely to reside in states with a higher proportion of population with high school education (81.0% vs. 80.6%, p=0.031) compared with patients who did not have all-cause utilization.

No difference in provider specialty and completion of continuation phase were found when examining mental health-related utilization. Patients who had mental health-related utilization were more likely to be older (44.9 vs. 40.7, p<0.001), have prior hospitalization (15.7% vs. 5.9%, p<0.001), have a higher CDS (2.4, vs. 1.8, p<0.001), have pre-existing anxiety (14.7% vs. 8.1%, p=0.021), have pre-existing substance abuse (11.7% vs. 3.0%, p<0.001), and have initial treatment during the first quarter of year (29.9% vs. 19.2%, p=0.012) compared with patients who did not have mental health-related utilization. Patients who had mental health-related utilization were more likely to reside in states with a higher median household income ($42,783 vs. $41,822, p=0.013) and in states with a higher

proportion of population with high school education (81.5% vs. 80.6%, p=0.003) than patients without mental health-related utilization.

Table 4.20 presents baseline characteristics between patients who had hospitalization during the one-year period after the continuation phase and patients who did not. For all-cause hospitalization, no differences were found in provider specialty and completion of continuation phase antidepressant treatment. Patients who had all-cause hospitalization were more likely to be older (45.6 vs. 40.5, p<0.001), have prior hospitalization (16.8% vs. 5.4%, p<0.001), have a higher CDS (2.4 vs. 1.8, p<0.001), have pregnancy-related visits during continuation phase (7.8% vs. 0.4%, p<0.001), have pre-existing anxiety (15.6% vs. 7.8%, p=0.001), and have pre-existing substance abuse (6.6% vs. 3.2%, p=0.022) compared with patients who did not have all-cause hospitalization. Patients who had all-cause hospitalization were more likely to reside in states with a higher median household income ($42,469 vs. $41,815, p=0.035) than patients without all-cause hospitalization.

No differences were found in provider specialty and completion of continuation phase antidepressant treatment for mental health-related hospitalization. Patients who had mental health-related hospitalization were more likely to be older (47.5 vs. 40.7, p<0.001), have prior hospitalization (19.7% vs. 5.9%, p<0.001), have a higher CDS (2.4 vs. 1.8, p<0.001), have pre-existing anxiety (18.3% vs. 8.1%, p=0.002), have pre-existing substance abuse (8.5% vs. 3.3%, p=0.02), and have the initial treatment in the first quarter of year (33.8% vs. 19.2%, p=0.002) compared with patients who did not have mental health-related hospitalization. Patients who had mental health-related hospitalization were more likely to reside in states with a higher median household income ($43,055 vs. $41,827, p=0.008) and

in states with a higher proportion of population with high school education (81.5% vs. 80.6%, p=0.012) than patients without mental health-related hospitalization.

Table 4.19 Baseline Characteristics between Patients Who Had Utilization and Patients Who Did Not for Continuation Phase Analysis

	All-cause Utilization			Mental Health-related Utilization		
	Had Utilization	No Utilization	P-value	Had Utilization	No Utilization	P-value
Number of observations	335	1,586		102	1,819	
% of sample	17.4	82.6		5.3	94.7	
Primary care provider (%)	52.2	60.1	0.008	48.0	59.4	0.024
Psychiatrist (%)	42.1	34.9	0.012	49.0	35.4	0.005
Non-psychiatric specialist (%)	5.7	45.0	0.602	2.9	5.2	0.308
Complete continuation phase antidepressant treatment (%)	45.4	44.8	0.839	47.1	44.8	0.648
Age	42.5 (12.6)	40.6 (11.8)	0.008	44.9 (12.7)	40.7 (11.9)	<0.001
Age categories (%)						
18-34	27.5	29.8	0.389	18.6	30.0	0.014
35-49	45.1	47.9	0.343	51.0	47.2	0.460
50-64	22.7	20.1	0.290	23.5	30.4	0.446
≥65	4.8	2.1	0.006	6.9	2.4	0.005
Male (%)	33.7	34.3	0.842	40.2	33.9	0.190
Median income in state of residence	42,197 (3,619)	41,804 (3,860)	0.087	42,783 (3,378)	41,822 (3,839)	0.013
% population with high school education in state of residence	81.0 (3.0)	80.6 (3.1)	0.031	81.5 (2.6)	80.6 (3.1)	0.003
Region (%)						
East North Central	33.1	28.9	0.127	38.2	29.2	0.052
East South Central	3.0	3.9	0.488	2.0	3.8	0.340
Middle Atlantic	2.1	2.6	0.597	2.0	2.5	0.721
Mountain	4.5	4.9	0.769	6.9	4.7	0.314
New England	6.0	3.8	0.069	2.9	4.2	0.525
Pacific	1.5	3.2	0.088	0	3.1	0.072
South Atlantic	26.3	30.8	0.102	25.5	30.2	0.309
West North Central	16.7	12.7	0.052	18.6	13.1	0.114
West South Central	6.9	9.3	0.159	3.9	9.1	0.072
Prior Hospitalization (%)	12.8	5.1	<0.001	15.7	5.9	<0.001
Pregnancy visits during continuation phase (%)	3.9	0.4	<0.001	2.0	1.0	0.347
Chronic disease score	2.1 (1.1)	1.7 (0.8)	<0.001	2.4 (1.1)	1.8 (0.8)	<0.001
Anxiety (%)	11.0	7.9	0.064	14.7	8.1	0.021
Substance abuse (%)	5.4	3.1	0.038	11.7	3.0	<0.001
Quarter of year of treatment initiation (%)						
Quarter 1	22.7	19.1	0.134	29.4	19.2	0.012
Quarter 2	10.1	19.5	0.874	13.7	19.7	0.135
Quarter 3	29.0	30.0	0.718	27.5	29.9	0.598
Quarter 4	29.3	31.5	0.427	29.4	21.2	0.709

Standard deviation in parentheses for continuous variables

Table 4.20 Baseline Characteristics between Patients Who Had Hospitalization and Patients Who Did Not for Continuation Phase Analysis

	All-cause Hospitalization			Mental Health-related Hospitalization		
	Hospitalized	Not Hospitalized	P-value	Hospitalized	Not Hospitalized	P-value
Number of observations	167	1,754		71	1,850	
% of sample	8.7	91.3		3.7	96.3	
Primary care provider (%)	56.3	59.0	0.495	53.5	59.0	0.360
Psychiatrist (%)	36.5	36.1	0.910	43.7	35.8	0.178
Non-psychiatric specialist (%)	7.2	4.9	0.200	2.8	5.2	0.373
Complete continuation phase antidepressant treatment (%)	50.9	44.3	0.101	53.5	44.5	0.135
Age	45.6 (13.5)	40.5 (11.8)	<0.001	47.5 (12.8)	40.7 (11.9)	<0.001
Age categories (%)						
18-34	21.6	30.2	0.020	12.7	30.1	0.002
35-49	41.3	48.0	0.098	47.9	47.4	0.936
50-64	28.7	19.8	0.006	31.0	20.2	0.027
≥65	8.4	2.1	<0.001	8.5	2.4	0.002
Male (%)	31.7	34.4	0.482	36.6	34.1	0.662
Median income in state of residence	42,469 (3,950)	41,815 (3,805)	0.035	43,055 (3,547)	41,827 (3825)	0.008
% population with high school education in state of residence	81.0 (3.2)	80.6 (3.1)	0.165	81.5 (2.9)	80.6 (3.1)	0.012
Region (%)						
East North Central	27.5	29.9	0.529	32.4	29.6	0.609
East South Central	2.4	3.8	0.351	2.8	3.7	0.689
Middle Atlantic	4.1	2.3	0.142	2.8	2.5	0.861
Mountain	6.6	4.6	0.255	8.5	4.7	0.141
New England	6.6	3.9	0.101	4.2	4.2	0.979
Pacific	2.4	3.0	0.676	0	3.0	0.137
South Atlantic	21.6	30.8	0.013	21.1	30.3	0.097
West North Central	18.6	12.9	0.042	22.5	13.1	0.022
West South Central	10.2	8.7	0.527	5.6	9.0	0.331
Prior Hospitalization (%)	16.8	5.4	<0.001	19.7	5.9	<0.001
Pregnancy visits during continuation phase (%)	7.8	0.4	<0.001	2.8	1.0	0.133
Chronic disease score	2.4 (1.2)	1.8 (0.8)	<0.001	2.4 (1.1)	1.8 (0.8)	<0.001
Anxiety (%)	15.6	7.8	0.001	18.3	8.1	0.002
Substance abuse (%)	6.6	3.2	0.022	8.5	3.3	0.020
Quarter of year of treatment initiation (%)						
Quarter 1	25.2	19.2	0.065	33.8	19.2	0.002
Quarter 2	14.4	19.9	0.085	11.3	19.7	0.077
Quarter 3	28.7	29.9	0.760	23.9	20.0	0.273
Quarter 4	31.7	31.0	0.847	31.0	31.1	0.986

Standard deviation in parentheses for continuous variables

4.4.2.2 Multivariate Logistic Analyses

Table 4.21 presents the odds ratios for utilization of continuation phase model. Patients initially prescribed an antidepressant by psychiatrists were more likely to have all-cause utilization (OR=1.34, 95% CI=1.05-1.79). Patients who had pregnancy-related visits during continuation phase were much more likely to have all-cause utilization (OR=11.2, 95% CI=4.09-30.4). Prior hospitalization and higher CDS increased the likelihood of having all-cause utilization (OR=1.89, 95% CI=1.22-2.93 and OR=1.47 95% CI=1.28-1.69, respectively).

In the model evaluating mental health-related utilization, both provider specialty and completion of continuation phase antidepressant treatment were not significant. Higher CDS (OR=1.77, 95% CI=1.45-2.17), and pre-existing substance abuse (OR=2.68, 95% CI=1.28-5.58) increased the odds of having mental health-related utilization, while initial treatment during the second quarter of year decreased the likelihood (OR=0.43, 95% CI=0.22-0.84).

Table 4.22 presents the odds ratios and 95% confidence intervals for hospitalization of continuation phase model. Provider specialty and completion of continuation phase antidepressant treatment were not significant. Patients older than 65 year were more likely to have all-cause hospitalization compared with patients aged 18-34 (OR=3.15, 95% CI=1.38-7.21). Patients who had pregnancy-related visits during continuation phase were more likely to have all-cause hospitalization (OR=46, 95% CI=14.9-142.7). Prior hospitalization and a higher CDS increased the likelihood of having all-cause hospitalization (OR=2.07, 95% CI=1.21-3.53 and OR=1.68, 95% CI=1.43-1.98, respectively) while initial treatment during second quarter of year (OR=0.50, 95% CI=0.28-0.90) decreased the lielihood of having all-cause hospitalization.

In the model evaluating mental health-related hospitalization, provider specialty and completion of continuation phase antidepressant treatment were not significant. Patients older than 65 year were more likely to have mental health-related hospitalization compared with patients aged 18-34 (OR=3.83, 95% CI=1.14-12.8). Pregnancy-related visits during continuation phase (OR=6.16 95% CI=1.29-29.43), a higher CDS (OR=1.85, 95% CI=1.47-2.32) increased the likelihood of having mental health-related hospitalization, while initial treatment in the second quarter of year (OR=0.30, 95% CI=0.13-0.68) or the third quarter of year (OR=0.46, 95% CI=0.23-0.89) decreased the likelihood of having mental health-related hospitalization.

Table 4.21 Logistic Regressions for Utilization after Continuation Phase

		All-cause Utilization		Mental Health-related Utilization	
Variable	Category	Odds Ratio	95% CI	Odds Ratio	95% CI
Primary care provider		Reference		Reference	
Psychiatrist		1.34	(1.05-1.79)	1.71	(1.10-2.66)
Non-psychiatric specialist		1.19	(0.69-2.05)	0.61	(0.19-1.98)
Completed continuation phase		0.96	(0.75-1.23)	0.97	(0.65-1.46)
Age group	18-34	Reference		Reference	
	35-49	1.00	(0.74-1.35)	1.46	(0.83-2.56)
	50-64	0.97	(0.67-1.40)	1.13	(0.57-2.24)
	≥65	1.56	(0.78-3.11)	2.40	(0.88-6.60)
Male		0.97	(0.75-1.26)	1.15	(0.74-1.78)
Income (in per 1000)		1.01	(0.96-1.07)	1.04	(0.96-1.13)
% with high school education		0.97	(0.90-1.04)	1.03	(0.92-1.15)
Region	East North Central	1.59	(1.01-2.51)	1.48	(0.69-3.16)
	East South Central	0.96	(0.47-2.14)	1.08	(0.21-5.50)
	Middle Atlantic	0.84	(0.36-1.93)	0.61	(0.11-3.32)
	Mountain	1.36	(0.65-2.84)	1.65	(0.46-5.94)
	New England	1.94	(0.96-3.92)	0.72	(0.15-3.42)
	Pacific	0.55	(0.19-1.59)	-	
	South Atlantic	Reference		Reference	
	West North Central	1.67	(1.01-2.76)	1.59	(0.67-3.76)
	West South Central	0.82	(0.47-1.45)	0.63	(0.18-2.22)
Pregnancy visits during continuation phase		11.16	(4.09-30.40)	3.04	(0.61-15.13)
Prior Hospitalization		1.89	(1.22-2.93)	1.31	(0.67-2.55)
Chronic disease score		1.47	(1.28-1.69)	1.77	(1.45-2.17)
Anxiety		1.14	(0.75-1.74)	1.27	(0.80-2.32)
Substance abuse		1.15	(0.62-2.13)	2.68	(1.28-5.58)
Quarter of year	Quarter 1	Reference		Reference	
	Quarter 2	0.83	(0.57-1.29)	0.43	(0.22-0.84)
	Quarter 3	0.86	(0.61-1.21)	0.61	(0.35-1.06)
	Quarter 4	0.78	(0.56-1.10)	0.61	(0.35-1.05)
Sample size=1,921					
	c-statistics=0.66			c-statistics=0.74	

Note: Pacific region merged to reference region due to perfect prediction

Table 4.22 Logistic Regressions for Hospitalization after Continuation Phase

		All-cause Hospitalization		Mental Health-related Hospitalization	
Variable	Category	Odds Ratio	95% CI	Odds Ratio	95% CI
Primary care provider		Reference		Reference	
Psychiatrist		1.03	(0.71-1.49)	1.37	(0.81-2.30)
Non-psychiatric specialist		1.34	(0.66-2.74)	0.45	(0.12-1.73)
Completed continuation phase		1.24	(0.88-1.73)	1.22	(0.76-1.98)
Age group	18-34	Reference		Reference	
	35-49	1.21	(0.76-1.91)	2.09	(0.97-4.51)
	50-64	1.59	(0.95-2.66)	2.24	(0.94-5.36)
	≥65	3.15	(1.38-7.21)	3.83	(1.14-12.83)
Male		0.93	(0.64-1.34)	0.97	(0.57-1.65)
Income (in per 1000)		1.07	(0.99-1.15)	1.09	(0.99-1.21)
% with high school education		0.95	(0.86-1.06)	1.02	(0.90-1.17)
Region	East North Central	1.30	(0.68-2.46)	1.29	(0.50-3.34)
	East South Central	1.18	(0.34-4.02)	2.42	(0.43-13.42)
	Middle Atlantic	1.94	(0.74-5.04)	0.96	(0.17-5.62)
	Mountain	2.10	(0.80-5.53)	2.05	(0.48-8.73)
	New England	1.94	(0.73-5.16)	0.98	(0.17-5.81)
	Pacific	0.89	(0.25-3.11)	-	
	South Atlantic	Reference		Reference	
	West North Central	1.87	(0.93-3.76)	2.03	(0.74-5.58)
	West South Central	1.80	(0.88-3.66)	1.33	(0.37-4.83)
Pregnancy visits during continuation phase		46.03	(14.85-142.7)	6.16	(1.29-29.43)
Prior Hospitalization		2.07	(1.21-3.53)	1.88	(0.89-3.99)
Chronic disease score		1.68	(1.43-1.98)	1.85	(1.47-2.32)
Anxiety		1.53	(0.90-2.59)	1.55	(0.76-3.14)
Substance abuse		1.37	(0.63-2.96)	1.37	(0.52-3.56)
Quarter of year	Quarter 1	Reference		Reference	
	Quarter 2	0.50	(0.28-0.90)	0.30	(0.13-0.68)
	Quarter 3	0.78	(0.50-1.22)	0.46	(0.23-0.89)
	Quarter 4	0.74	(0.47-1.17)	0.54	(0.29-1.01)
Sample size=1,921					
	c-statistic=0.76			c-statistic=0.79	

Note: Pacific region merged to reference region due to perfect prediction

4.4.2.3 Propensity Score Matching

Logistic regressions were run on the matched sub-sample who completed acute phase (N=1,121). The coefficient of psychiatrist became insignificant for mental health-related utilization model after the matching, which is likely due to decrease in sample size (Table 4.23) .Odds ratios were consistent before and after the matching since the confidence intervals overlapped.

Table 4.23 Odds Ratios of Utilization and Hospitalization for Continuation Phase Model before and after Propensity Score Matching

Variable	Utilization		Hospitalization	
	All-cause	Mental Health-related	All-cause	Mental Health-related
	Pre-matching			
	N=1,921			
Primary care provider	Reference	Reference	Reference	Reference
Psychiatrist	1.37* (1.05-1.79)	1.71* (1.10-2.66)	1.03 (0.71-1.49)	1.37 (0.81-2.31)
Non-psychiatric specialist	1.19 (0.69-2.05)	0.61 (0.19-1.98)	1.34 (0.66-2.74)	0.45 (0.12-1.73)
Completed continuation phase	0.96 (0.75-1.23)	0.97 (0.65-1.46)	1.24 (0.88-1.73)	1.22 (0.76-1.98)
	Post-matching			
	N=1,121			
Primary care provider	Reference	Reference	Reference	Reference
Psychiatrist	1.41* (1.03-1.95)	1.68 (0.88-3.23)	1.21 (0.74-1.97)	1.49 (0.74-2.98)
Non-psychiatric specialist	-	-	-	-
Completed continuation phase	0.94 (0.68-1.30)	1.80 (0.95-3.40)	1.43 (0.88-2.31)	1.72 (0.87-3.42)

Note: 95% CI in parentheses. Regressions include all the covariates listed in Table 4.21 and Table 4.22
*p<0.05

In summary, we found patients initially prescribed an antidepressant by psychiatrists has higher risk of all-cause and mental health-related utilization during the one-year period after the continuation phase, and we did not find an effect of completion of continuation phase on utilization or hospitalization.

CHAPTER V

DISCUSSION

This Chapter discusses the findings of each aim and its policy and clinical implication (Section 5.1), observed confounding and propensity score matching (Section 5.2), strength and limitations (Section 5.3-5.4), future research (Section 5.5), and conclusion (Section 5.6).

5.1 Discussion for Each Aim and Its Policy and Clinical Implications

5.1.1 Aim 1

To examine characteristics among patients initially prescribed an antidepressant by providers with different specialties to treat major depressive disorder (MDD)

In Aim 1, we found differences among patients initially prescribed an antidepressant by providers with different specialties. Prior literature has suggested that psychological sickness is the strongest predictor for mental health specialty care.[46] Although we did not have a direct measure of psychological sickness of the study population, comorbid psychological conditions of anxiety and substance abuse identified in the 6-month pre-index date period were strong predictors for initial antidepressant treatment with psychiatrists. On the other hand, Chronic Disease Score (CDS) which measures overall comorbidities was the strongest predictor to receive an initial antidepressant prescription from non-psychiatric specialists. These results are consistent with the role of which specialists were designated for treating patients with more needs for specialty care. We also found prior specialty care is a strong predictor of initiate prescriber for antidepressant treatment. This might indicate that these patients had better access to specialty care since they had been using it. It could also represent a pre-existing relationship with specialists which in turn increase the likelihood to initiate treatment with them. We do not have information on whether the insurance policy requires gatekeeping for each individual. Since the majority of our study population is under fee-for-service plans, prior specialty experience could be a good proxy for access.

The findings from Aim 1 underscore the importance of including patient characteristics in analyses examining provider specialty differences in order to eliminate potential biases. In light of these results, interpretation of provider specialty effects in Aim 2

and Aim 3 must be made with caution. Depending on how much the residual patient differences were left in the error term and how that influenced the outcomes in Aims 2 and Aim 3, interpretation of results from those aims must be made with consideration of patient effects as well.

5.1.2 Aim 2

To examine the association of antidepressant treatment with initial prescriber specialty and receipt of guideline-concordant outpatient follow-up visits among patients with MDD

We first discuss the factors associated with receipt of guideline-concordant follow-up visits (Section 5.1.2.1). Next, we discuss the predictors for completion of antidepressant treatment phases (Section 5.1.2.2). Provider specialty is the explanatory variable of interest.

5.1.2.1 Provider Specialty and Receipt of Guideline-concordant Follow-up Visits

We found that only 31% of patients received guideline-concordant follow-up visits in our study population, which is similar to prior studies using the same HEDIS criteria[4, 6, 49], but higher than NCQA's report[115] (Table 5.1). In this dissertation, we only included patients with an MDD diagnosis while other studies have also included patients with dysthymia or depressive disorder not otherwise specified.[4, 6, 49]

Table 5.1 Comparison of Proportion of Receipt of Guideline-concordant Follow-up Visits

Data Source	Study Year(s)	Study Population	Percentage
Present study	*2000-2004*	*Commercially insured*	*31*
Robinson[6]	2001-2004	Commercially insured	39
Morrato[49]	1998-2005	Commercially insured	40
Jones[4]	1997-2005	VA	27
NCQA	2001	Commercially insured	19.8
NCQA	2002	Commercially insured	19.2
NCQA	2003	Commercially insured	20.3
NCQA	2004	Commercially insured	20.0

Frequent follow-up provides opportunities for providers to monitor side effects and clinical response and to educate patients about the treatment. For patients taking antidepressants to treat MDD, it is especially important to promote adherence as they may discontinue because of the time required to achieve response, or they may stop taking the

antidepressants once they start feeling better.[116] Improvement for follow-up care should be taken into action particularly given the positive association with antidepressant completion.

Not only the rate for guideline-concordant follow-up visits is low in general, we found that older patients (greater than 50 years old) are at risk of less frequent follow-up. Clinicians should pay special attention to this demographic group in their practice when they schedule follow-up visits. Interventions such as case management should also target this group where there is still much room for improvement. In addition, we also found that patients under burden of higher out-of-pocket copayment were less likely to have guideline-concordant follow-up visits. Insurance plans should bear in mind the adverse consequences in follow-up care for the depressed patients when undergoing reform with cost-containment strategies.

We found that initial treatment by a psychiatrist was the strongest predictor of receipt of guideline-concordat follow-up visits, which is consistent with studies by Robinson et al. and Jones et al even though they used different definitions for provider specialty.[4, 6] We controlled for as many patient characteristics as were available, so the difference we observed is largely attributable to provider effect. Although we can not examine why such differences exist based on the data we have, the findings warrant the need to improve follow-up for patients with depression managed in primary care settings. It is probably neither efficient nor realistic to channel all the depressed patients into specialty care. Focuses should be to improve management for depression in primary care, and many interventions have been examined in randomized controlled trials.[117] The positive association found between initial prescription from a psychiatrist and guideline-concordant follow-up is suggestive for a greater degree of integration between primary and secondary care with consultation-liaison.

To test how the results may vary based on the definition used to identify follow-up visits, we conducted two sensitivity analyses. The HEDIS measures include follow-up visits made to providers without prescribing privileges such as psychologists. To count the visits more relevant to antidepressant management, we included only those visits made to providers with prescribing privileges as the outcome in the first sensitivity analysis. The odds ratios and significance of provider specialty were similar to the main analysis. Second, we identified the visits that were made to the provider who wrote the initial antidepressant prescription regardless of diagnosis. Visits made to the same provider who wrote the prescription provided an opportunity for patients to talk about antidepressant treatment, although it might not be the main reason for the visits. The odds ratios for psychiatrists became smaller and the difference between non-psychiatric specialists and PCPs diminished. Our conclusion that initiating antidepressant treatment with a psychiatrist was associated with greater likelihood of receipt of guideline-concordant follow-up visits did not change (Table 4.6). These sensitivity analyses give us confidence that there is a systematic difference between patients initially prescribed by primary care providers (PCPs) and patients initially prescribed by psychiatrists. The findings from these sensitivity analyses could be also indicative that the HEDIS measures provide an upper bound when examining follow-up visits, and alternative approaches may be worth exploring.

5.1.2.2 Antidepressant Treatment in the Real World

We found that acute phase antidepressant treatment completion was suboptimal (46.8%), which mirrors the results of several prior studies (Table 5.2). The proportion of patients who completed acute phase antidepressant treatment based on empirical analyses is 45-50% for commercially insured population.[2, 6] The proportion was much lower in a VA sample (11%)[4] and slightly higher based on NCQA historical reports.[115]

Table 5.2 Comparison of Proportion of Acute Phase and Continuation Phase Completion

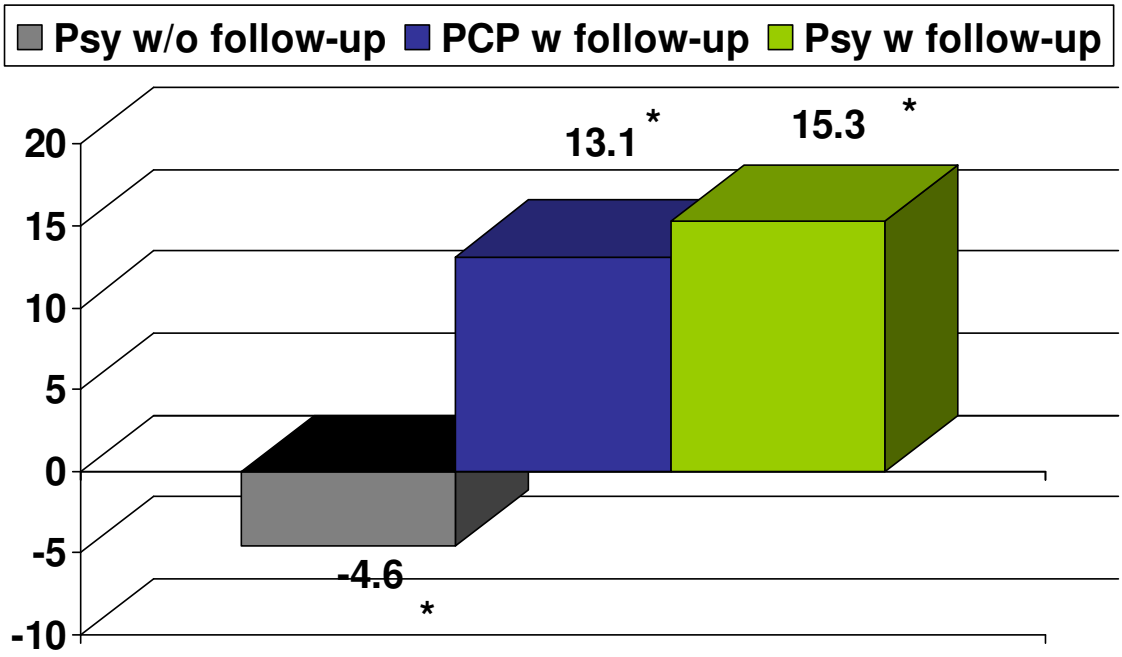
Data Source	Study Year(s)	Study Population	Acute phase completion (%)	Continuation phase completion (%)
Present study	*2000-2004*	*Commercially insured*	*46.8*	*44.9*
Robinson[6]	2001-2004	Commercially insured	46.8	44.3
Akincigil[2]	2003-2005	Commercially insured	51	41.5
Jones[4]	1997-2005	VA	11	N/A
NCQA	2002	Commercially insured	56.9	36.8
NCQA	2003	Commercially insured	59.8	37.7
NCQA	2004	Commercially insured	60.7	39.2

The association between provider specialty and antidepressant adherence is not consistent in the literature. Five of the ten studies we examined in the literature review found that mental health specialty care significantly increased the likelihood of antidepressant treatment adherence.[2, 3, 6, 16, 17] We found that the provider effects are more complicated. This dissertation is the first to consider an interaction effect between provider specialty and receipt of guideline-concordant follow-up visits in a general population.

Patients who were initially prescribed an antidepressant by psychiatrists but failed to receive guideline-concordant follow-up visits were 4.6 percentage points less likely to complete the acute phase compared with patients initially prescribed an antidepressant by PCPs who did not have guideline-concordant outpatient follow-up visits (Figure 5.1). The marginal effect of guideline-concordant follow-up visits was 13.1 percentage points among patients initially prescribed by PCPs and 19.9 percentage points among patients initially

prescribed by psychiatrists. The combination of provider and follow-up effects results in a marginal effect of 15.3 percentage points for follow-up made by patients initially prescribed by psychiatrists compared with patients who were initially prescribed by PCPs and did not receive guideline-concordant follow-up visits (Figure 5.1).

Figure 5.1 Marginal Effects of Provider Specialty and Guideline-concordant Follow-up Visits on Probability of Acute Phase Antidepressant Completion



Note: PCP without follow-up as reference group

If interpreting the effect of the interaction term as purely a provider effect, psychiatrists were more effective in encouraging patients to complete acute phase antidepressant treatment than PCPs when guideline-concordant follow-up visits were also delivered. Psychiatrists who failed to deliver guideline-concordant follow-up visits were less likely to have their patients completed the acute phase compared with PCPs who failed to deliver guideline-concordant follow-up visits.

Before jumping into a conclusion of divergent provider effects between patients who received guideline-concordant follow-up visits and patients who did not, one must consider

differences in patient cohorts between PCPs and psychiatrists, particularly since these variables are marginally significant. One major unobservable confounder is depression severity which is expected to be different between patient cohort treated by PCPs and by psychiatrists. Mental health specialists tend to encounter more severely depressed patients.[47] However, how severity influences antidepressant adherence is unclear. There could be two hypotheses in the opposite directions. Patients with higher need (in terms of greater severity) might be more motivated and more compliant to provider's direction regarding taking medications. On the other hand, severe depression itself might make patients resistant to any recommendations. It is possible that the latter group of patients may forego doctor's follow-up appointment and be reluctant to take their antidepressant as suggested. This scenario may be the reason why the marginal effect of psychiatrist is negative. To consider that even psychiatrists (who we hypothesized to have better skills and knowledge in treating depression) could not make those patients come for follow-up visits, it is probably not surprising how non-compliant these patients are in taking antidepressants. On the other hand, the more motivated patients treated by psychiatrists will comply with their doctor's recommendation and the existence of this group of patients makes the interaction effect of psychiatrist and receipt of follow-up visits significant. Without complete measurement of motivation and depression severity in our analysis, the provider effects we observed in these results may be partially attributable to patient differences.

We found a strong positive association between receipt of guideline-concordant follow-up visits and completion of acute phase antidepressant treatment. To our knowledge, this dissertation is the first study to examine this association in a commercially insured population. Only one study based on a VA population have examined this, and gave the

similar conclusion (OR=2.1, 95% CI=1.54-2.88).[4] In addition, we considered the interaction effect between guideline-concordant follow-up visits and provider specialty. Our empirical analyses suggest that follow-up visits may promote patient adherence to antidepressant treatment because patients who were initially prescribed an antidepressant by PCPs or by psychiatrists and had guideline-concordant follow-up visits were more likely to complete acute phase antidepressant treatment. Our findings underscore the importance of providing frequent follow-up care to encourage patients to adhere to acute phase antidepressant treatment.

We also examined completion of antidepressant treatment in the continuation phase on the sub-sample of patients who completed acute phase (n=1,921). The interpretation of the results is conditional on acute phase completion. As with acute phase completion, completion of continuation phase was suboptimal (45%, Table 5.2) Prior studies found that the proportion of continuation phase completion ranged from 35-45% based on the HEDIS measures.[6, 115] Akincigil et al. constructed continuation phase completion in a similar way to consider that only those who completed acute phase entered into continuation phase. Their findings were very similar to ours, even though the threshold of MPR was lower in their study (75%). Among the patients who completed acute phase and entered into continuation phase, we found no differences in continuation phase antidepressant completion by provider specialty. Our study is the first to attempt to measure and evaluate follow-up visits during continuation phase. We found that having three or more follow-up visits during continuation phase was associated with antidepressant completion. It is suggestive that frequent follow-up is not only effective during the initiation of the treatment, but also important in a long run.

The sub-optimal rate of guideline-concordant antidepressant treatment remains a challenging problem. The results from the dissertation support the need for innovative protocols and interventions to achieve better care for depressed patient for post-prescription monitoring and management. Several strategies including collaborative care and case management that have been systematically evaluated to be effective in improving antidepressant adherence and depression clinical outcomes.[117-119] Improvement can be targeted at two arenas for potential change. The first is organizational including a better systems of referral, collaboration programs, and on-site access to psychiatrists in primary care settings.[120, 121] Case management with telephone medication counseling delivered by nurses or trained counselor and pharmacist-provider prescribing information exchange have been shown to be effective, and may involve minimum system change.[117] The second is provider changes via physician education, psychiatric diagnostic screening tools, and increased consulting time.[122] Multifaceted interventions with combination of two could be beneficial too.[123]

5.1.2.3 Aim 3

To examine the association of subsequent healthcare utilization with initial prescriber specialty and antidepressant treatment among patients with MDD

In Aim 3, we sought to understand the association between provider specialty, antidepressant treatment completion and subsequent healthcare utilization (hospital admissions and emergency room visits). Our results suggest that patients initially prescribe an antidepressant by psychiatrists were more likely to have all-cause and mental health-related utilization, and patients initially prescribed an antidepressant by non-psychiatric specialists were more likely to have all-cause utilization. Patient's needs for healthcare are probably the main driving force of healthcare utilization, and need variables in our study (CDS in all-cause utilization model; anxiety and substance abuse in mental health-related utilization model) were indeed significant predictors. After controlling for comorbidity to adjust for patient case-mix, we still found a significant difference between PCPs and specialists as in prior literature.[124] When we limited the outcome to hospitalization, only patients treated by non-psychiatric specialists were statistically significantly more likely to have all-cause hospitalization during one year following the end of acute phase. Inconsistent effects between utilization model and hospitalization model indicate that the difference found in utilization between patients initially prescribed an antidepressant by psychiatrists and patients initially prescribed an antidepressant by PCPs may be driven largely by emergency room visits.

We found a protective effect of acute phase antidepressant treatment completion over all-cause utilization, mental health-related utilization, and all-cause hospitalization. This is consistent with a study conducted on a VA sample that found patients with adequate duration

of antidepressant treatment were significantly less likely to have all-cause hospitalization.[18] We failed to find an association between acute phase antidepressant treatment completion and mental health-related hospitalization as in this prior study.[18] It might be due to the possibility that our study population is relatively mentally healthier than the VA population. For example, the rareness of mental health-related hospital admissions (3-4%) in our sample compared with the VA sample (7.6%) in this prior study prevents us from detecting the difference.[18]

This dissertation is the first to examine the association between provider specialty, continuation phase antidepressant completion and subsequent healthcare utilization. Only the psychiatrist variable remained significant in the continuation model that evaluated all-cause and mental health-related utilization. There are two possible reasons why we observed inconsistent results of provider specialty between acute phase model and continuation phase model. First, only those who completed the acute phase antidepressant treatment entered the continuation phase model, which substantially reduced the sample size and the power to detect differences. Also, there was a nine-month gap (acute phase plus continuation phase) between index date and the period where we identified utilization in the continuation phase model. Such lag in time may weaken the association because patients may have stopped seeing the provider or changed to another provider during this period.

In the sub-population that completed the acute phase, we were not able to find any significant effect of continuation phase antidepressant treatment completion on subsequent healthcare utilization or hospitalization. The explanation could be that, from a clinical stand point, acute phase aims at achieving remission. Acute phase completion should help patients eliminate depressive symptoms and allow them to restore mental health. This stage of

antidepressant treatment is more vital in a patient's mental self-being, and the mental state might be influential to other physical conditions as well, which results in difference in subsequent utilization. Once entering into continuation phase, patients were assumed to be remitted. The purpose of continuation phase antidepressant treatment is to prevent relapse. With the absence of depressive symptoms in the sub-population who completed the acute phase, there might not be any effect of continuation phase over subsequent utilization.

The empirical evidence of the protective effect of acute phase antidepressant treatment over the risk of subsequent healthcare utilization and hospitalization found in this dissertation translates guideline-recommended antidepressant use into improved health by reduction of costly adverse events. Our findings support the theory that the increase expenditures associated with antidepressant prescription early on may be offset by reductions in the costs of hospitalizations. In addition to clinical effectiveness, antidepressant therapy is economically effective in treating MDD if utilized properly based on guideline recommendations. When planning the intervention to promote antidepressant adherence, policymakers should factor the potential cost-saving associated with antidepressant adherence to budget and allocate the resources.

5.2 Observed Confounding and Propensity Score Matching

This dissertation utilized propensity score matching which gives a comparable cohort between patient initially prescribed an antidepressant by PCPs and patient initially prescribed an antidepressant by psychiatrists in observable variables and potentially unobservable confounders as well. After propensity score matching, the distribution of severity among patients between groups should, ideally, become similar.

In Aim 2 analyses, the findings are consistent before and after the matching for the model that evaluates guideline-concordant follow-up visits. In the model that evaluates acute phase antidepressant treatment completion, we found that the psychiatrist coefficient and its interaction term with guideline-concordant follow-up visits became insignificant after the matching. Two reasons may explain the inconsistent findings. First, these variables were at marginal significance in the original model. The decrease in sample size after the matching may decrease the power to detect the differences. Second, the interaction effect may be more profound among the patients who we were unable to find matches and were likely to be more severely ill. Exclusion of these patients in the propensity score matched population may preclude us from observing the significant effect. The findings are consistent before and after the matching for the model that evaluates continuation phase antidepressant treatment completion.

In Aim 3 analyses, we had similar findings before and after the matching, except that we had an inconsistent finding of the protective effect of acute phase completion over all-cause and mental health-related utilization. There could be three explanations. First, the reduction of the sample size resulted in losing power to detect differences. Second, acute phase completion might be more effective over a population that was eliminated during the

process of propensity score matching. Third, after examination of the principal diagnosis for utilization, we found that they were largely from emergency room visits where the causes were somewhat minor and less concentrated. The effect of acute phase completion might not be homogenous between more severe events like hospitalization and more minor events like emergency room visits. Combination of these two as an outcome might dilute the true effect over hospitalization that was consistently found before and after the matching.

5.3 Limitations

This dissertation has several limitations. Since the source of information came from claims data, the validity of study results depends on the coding accuracy. We included patients who were diagnosed with major depressive disorder with a single episode (ICD-9 code 296.20-296.24). Our intension was to identify new patients who were naïve users of antidepressant. Even though we have utilized data from 6-month prior to identify our target population, the tendency of how providers distinguish and code new and recurrent episodes of MDD could be influential for our sample inclusion process. In addition, the follow-up visits were identified based on service claims that had a mental health diagnosis code. If this piece of information was not coded accurately, it will influence the results particularly with regard to receipt of guideline-concordant follow-up visits and provider specialty. Depression is a common disease that is being under-diagnosed, and patients might not want it be recorded due to stigma.[22] Some visits to manage antidepressant treatment might not be coded as such, and some visits coded for another purpose might include evaluation of antidepressant treatment. How such a scenario could influence our findings has been addressed by sensitivity analyses. Even though we were able to investigate the timing and frequency of follow-up visits, we were not able to know the quality of individual visits. In addition, the data provide no information on whether the follow-up visits have been scheduled, cancelled or missed.

The prescription claims data only provide information on prescription refill patterns instead of actual medication use. Medication refill records do not necessarily reflect consumption of the medication. Samples from the doctors, pill splitting, and obtaining medication purely with out-of-pocket costs can not be observed in this data. Despite those

shortcomings, using prescription claims data to measure medication adherence remains valid and reliable.[84] We constructed antidepressant treatment according to guideline recommendations. However, we could not distinguish the cases where the discontinuation was clinically appropriate and approved by providers.

In the analytical model, we included state level median household income and percentage of population with high school education as proxies for socio-economic status. These state level data may only partially controlled for socio-economic status, and also limit the interpretation of these variables. We do not have provider variables such as gender, year of practice, practice setting, and patient volume in our data. These provider variables may be influential to the outcomes we examined. Insurance plan variables are limited, too. We do not have the benefit structure of each individual, and we were only able to create several proxies based on claims level information. In addition, we did not have information on whether any organizational intervention such as disease management and information technology has been implemented. These factors could affect both provider and patient behavior.

Several hypothesized mechanisms of provider differences discussed in Chapter II are attitudes toward depression, knowledge about treatment and guidelines, and competing demand. Unfortunately, it is impossible to tell which mechanism is responsible for the provider effects, if any, from the current dataset. However, examining the total effect is still crucial for the purpose of this dissertation. Provider differences were found for guideline-concordant follow-up visits and subsequent healthcare utilization. These findings support our hypotheses and warrant further investigation to examine why such differences exist.

Power could be an issue too. Events such as mental health-related hospital admissions are rare in this relatively healthy population. The small number of cases may preclude us from detecting small differences.

Even though propensity score methods can increase efficiency to reduce bias, it still functions under the assumption that there are no unobservable confounders. This propensity score matching method can still lead to biased estimates if unobservable confounders exist. In addition, the success of propensity score adjustment requires substantial overlap between groups. Individuals that fall outside the region of common support have to be disregarded, but information from those individuals could be useful.

Our data are originated from a large national health plan affiliated with i3 Innovus. Even though we were able to have a sample size of four thousand individuals to analyze, our findings might not be generalized to the whole U.S. population. Our study population is based on commercially insured individuals. Results may be different for people under other insurance coverage such as Medicaid or Medicare. In addition, the majority of the patients in our sample were under fee-for-service reimbursement scheme (98.5%), and the findings from this dissertation may not be applied to individuals under Health Maintenance Organization. Our study also excluded children, patients with concurrent bipolar or schizophrenia, and patients who were on augmented antidepressant treatment, and our findings may not be applicable for these patients.

The most important limitation is that the observational design prohibits attribution of causality. Several potential unobservable patient characteristics have been discussed in Chapter II. If these unobservable variables are confounders which influence the independent variable of interest and the outcomes, it will lead to biased estimates. Unobservable patient

characteristics that might confound the provider effect include perceived stigma, attitude toward treatment for depression, and depression severity. Particularly, the absence of depression severity is a concern because it might directly impact both therapy decisions and the completion of the treatment.

5.4 Strengths

Despite the aforementioned limitations, this dissertation has several strengths. This dissertation contributes to the literature by carefully examining the relationship of several guideline components of antidepressant treatment within a geographically diverse commercially insured population. Our integrated data have comprehensive information for healthcare visits and prescriptions. The use of medication possession ratio and gap measure together incorporate both adherence and persistence in evaluation of antidepressant use.[85, 125]

There are several strengths of our analytical models. We identified the provider specialty based on index antidepressant claim. We considered this source to more accurately point toward the providers who managed antidepressant therapy compared with other sources such as clinic types and provider specialty based on medical visits used in some prior studies.[2-4, 6, 16, 43] Our study is the first to examine provider specialty and guideline-concordant follow-up visits simultaneously in a more generalized population. Only one study based on veterans incorporated both variables, and the findings were consistent with ours.[4] In addition, we further investigate the relationship of follow-up visits during continuation phase and antidepressant completion. To our knowledge, our study is the first to attempt to evaluate this relationship. The positive association found in our study can serve as a basis for hypothesis-generation to establish guidelines about the frequency of follow-up visits in continuation phase for antidepressant management. Our study is the first to evaluate whether daily regimen may influence antidepressant adherence. Patients who were required to take two or more pills a day were less likely to complete acute phase. This piece of evidence may be helpful for clinicians in choice of antidepressant agent. Finally, we used rigorous

methodologies including propensity score matching and sensitivity analyses to ensure the reliability of the reported findings.

5.5 Future Research

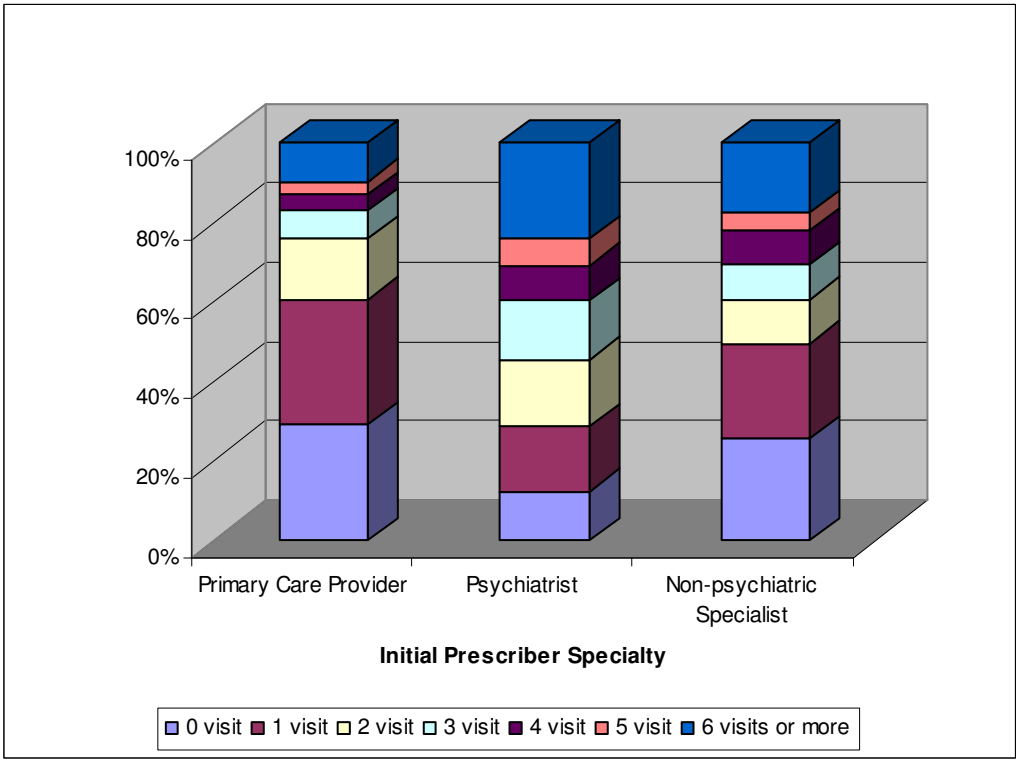
In this dissertation, we found differences in characteristics between patients initially prescribed an antidepressant by PCPs and patients initially prescribed an antidepressant by psychiatrists (Aim 1). The administrative data allow us to examine this question with a large sample size in a naturalistic setting. Future research should incorporate different data sources or data collecting techniques to enrich our understanding in this regard.

The findings from this dissertation suggest that follow-up visits are under-utilized for managing antidepressant treatment overall, particularly in primary care settings. This dissertation only points out that such difference exists, but can not answer the question of why because our data did not allow examination of the mechanisms that lead to such differences. The decision for follow-up visits could be driven by providers (whether recommendation of follow-up was given) and by patients (whether patients followed the recommendation and whether they have needs for follow-up). First, future research should use provider as the unit of analysis and systematically evaluate the differences in attitudes, knowledge, barriers and practice setting in treating depression with antidepressant between mental health specialists and primary care providers. Provider surveys could be a useful tool. In addition, studies should be conducted to examine how patient behavioral factors, such as attitude, knowledge, stigma, and clinical factors like depression severity may play a role. These studies could assist policymakers in understanding how to support primary care in providing more guideline-concordant care to depressed patients and to simulate effective organizational intervention to improve quality of care.

In the main analysis, completion of follow-up visits during the acute phase was defined using the HEDIS measures with at least three visits as a threshold,[36] which is

commonly used in the literature.[3, 4, 6, 7] However, three visits may be a minimum standard. The AHCRP depression guidelines[8] recommend that patients with more severe depression should be seen weekly for the first 6 to 8 weeks of acute treatment, and the APA also recommends that patients should be seen on a weekly basis during acute phase.[9] According to these guidelines, a patient should receive at least six follow-up visits based on a conservative calculation. Based on descriptive analysis from Aim 2, only 9.7% of patients initially prescribed an antidepressant by a PCP, 24.1% of patients initially prescribed an antidepressant by a psychiatrist, and 17.4% of patients initially prescribed an antidepressant by a non-psychiatric specialist has six or more visits (Figure 5.2). Future research should focus on assessing what level of follow-up care is cost-effective and clinically appropriate. In our sensitivity analyses, we demonstrated that the results may differ based on the approaches to identify follow-up visits. Using the HEDIS measures which require mental health diagnosis may underestimate follow-up visits in primary care setting where under-coding is more likely to occur. Future research should focus on developing an algorithm to more precisely measure the follow-up visits for depression.

Figure 5.2 Frequency of Follow-up Visits During Acute Phase



This is the first study to assess the association between receipt of guideline-concordant follow-up visits and antidepressant completion in a more generalized population. The positive association is not surprising, but it was disappointing that the overall rate of follow-up remains far from optimal. While performance measurement has become a prominent approach in both assessment and reimbursement in today's healthcare system, it is vital to have timely empirical evidence supporting its reliability, accuracy, and effectiveness. Our finding of the positive association between follow-up visits and acute phase completion is encouraging in this aspect. Even though our finding is promising, future research should also examine how quality of the follow-up visits, such as time spent with patients and communication style, influence antidepressant use to give a complete picture.

This dissertation showed that acute phase antidepressant completion significantly decreased the risk of all-cause hospitalization. Even though we failed to find an association

between continuation phase completion and subsequent utilization, future research should empirically test the effectiveness of continuation phase antidepressant treatment with depression relapse as an endpoint to evaluate whether it serves its desirable purpose.

5.6 Conclusion

Overall, the results of this dissertation are strongly suggestive of a large gap between clinical guideline recommendations and actual practice in treating MDD with antidepressant. We found only a small proportion of depressed patients received appropriate follow-up care for management of antidepressant treatment. There are differences between primary care and mental health specialty settings in follow-up visits, but why there were such differences requires further investigation. Many patients did not use antidepressant for a desirable duration. We found receipt of guideline-concordant follow-up visits was associated with completion of antidepressant, and frequent follow-up should be encouraged to promote adherence. We also observed a protective effect of acute phase completion over all-cause hospitalization. This empirical evidence provides economical justification of the cost offset of expenditures associated with antidepressant treatment. The results of this dissertation present valuable knowledge of health service research in treatment for MDD with antidepressant therapy. It is our hope that findings from this dissertation will simulate future research to benefit the well-being of patients with MDD.

APPENDIX

Appendix 1 DSM-IV criteria for major depressive episode

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. (Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.)
   1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
   2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
   3. Significant weight loss when not dieting or weight gain (e.g., a change of >5% of body weight in a month), or decrease or increase in appetite nearly every day
   4. Insomnia or hypersomnia nearly every day
   5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
   6. Fatigue or loss of energy nearly every day
   7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
   8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
   9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a mixed episode

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

D. The symptoms are not due to the direct physiologic effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism)

E. The symptoms are not better accounted for by bereavement; i.e., after the loss of a loved one, the symptoms persist for >2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation

Source: *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition. Washington, DC, American Psychiatric Association, 2000.

Appendix 2 Variables included in the original dataset

File	Variables
Membership	Patient encrypted identification, age, gender, region of residence, start and end observed date
Service claims	Patient encrypted identification, amount reimbursed, amount of co-payment, CPT procedure code, date of service, primary and secondary diagnosis codes, provider encrypted identification, provider specialty, place of service, encounter flag, benefit level of payment
Facility claims	Patient encrypted identification, amount reimbursed, amount of co-payment, CPT procedure code, date of service, primary and secondary diagnosis codes, primary and secondary procedure codes, provider encrypted identification, provider specialty, place of service, source of admission, diagnostic related group, encounter flag, participating provider indicator, revenue code, benefit level of payment
Prescription claims	Patient encrypted identification, brand name, National Drug Code (NDC), dosage, strength, days-of-supply, quantity dispensed, mail order, therapdate of service, cost amount of claim, amount of patient co-payment, encrypted provider identifier, and provider specialty

Appendix 3 Odds Ratios and Specification Tests for Continuation Phase Antidepressant Treatment Completion Model with Different Forms of Follow-up Visits

	Model 1	Model 2	Model 3
Continuation phase follow-up continuous	1.05 (1.02-1.08)		
Continuation phase follow-up binary			
0-2 visits		Reference	
3 or more visits		1.62 (1.31-2.02)	
Continuation phase follow-up categories			
0 visits			Reference
1-2 visits			1.67 (1.34-2.10)
3 or more visits			2.18 (1.70-2.79)
linktest (p-value) [§]	0.016	0.158	0.028

Note: the models have identical covariates except the forms of follow-up visits.
[§] insignificant indicates correct model specification without omitted variable misspecification

Appendix 4 Results of Specification Tests

Model	c-statistic	Linktest[§] (p-value)	Hosmer-Lemeshow[δ] (p-value)
Aim 2			
Guideline-concordant follow-up visits	0.72	0.685	0.329
Acute phase completion	0.63	0.053	0.223
Continuation phase completion	0.62	0.073	0.636
Aim 3			
Acute phase			
All-cause utilization	0.66	0.275	0.306
Mental health-related utilization	0.71	0.657	0.972
All-cause hospitalization	0.70	0.088	0.113
Mental health-related hospitalization	0.72	0.779	0.158
Continuation phase			
All-cause utilization	0.66	0.896	0.548
Mental health-related utilization	0.74	0.592	0.136
All-cause hospitalization	0.76	0.374	0.801
Mental health-related hospitalization	0.79	0.662	0.671

[§] insignificant indicates correct model specification without omitted variable misspecification
[δ] insignificant, which shows a good model fit

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