Summer 2014

Investigating effects of diagnosing depression among patients with acute myocardial infarction

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INVESTIGATING EFFECTS OF DIAGNOSING DEPRESSION AMONG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

by

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A thesis submitted in partial fulfillment
of the requirements for the Doctor of
Philosophy degree in Pharmacy
in the Graduate College of
The University of Iowa

August 2014

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PH.D. THESIS

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ACKNOWLEDGMENTS

I finally made it through graduate school with laughs, tears, and appreciation. Many people have supported and encouraged me during this challenging, but fruitful time in my life.

My parents, Ruying Tang and Xiumei Wang have supported me since I was born. Their unconditional love and guidance were invaluable to me. Moving from my hometown Beijing to Iowa City for graduate school was not easy for any of us and it has taken me further away from them, but I love them so much and feel their love every second in my life. I spent my first five years with grandparents, Xueyao Tang and Shufen Yang, who taught me how to be a good person and never give up big dreams when I was a kid. Grandpa passed away when I was in graduate school. I hope that in heaven, he could know that I learned a lot from him and how much I miss him.

I also want to specially thank my boyfriend, Brandon Patterson, who has given me constant support in the past few years. He is a smart, passionate, and loving man. Without him, I do not know how I could survive graduate school. I am looking forward to our future.

I would like to express my special appreciation and thanks to my advisor John Brooks throughout my graduate school. He has been a tremendous mentor to encourage my research and to allow me to grow as an independent scientist. He taught me what passion is from an enthusiastic and dedicated researcher. John has everything a graduate student needs from an advisor. My special thanks also go to Bill Doucette, Jill Kauer, Mary Schroeder, and George Wehby who have served as my committee members and provided constant support and advice on my dissertation and career development. I also want to extend my deep gratitude to many other faculties, Erica Ernst, Karen Farris, Amber Goedken, Linnea Polgreen, Bernard Sorofman, Julie Urmie, Matt Witry, and Yang Xie, who have helped me during my graduate school.

I want to thank many other colleagues at the College of Pharmacy for shaping my experiences in the past five years: Elizabeth Chang, Jayoung Han, Xiaoyun Pan, Puttarin Kulchaitanaroaj, An-Chen Fu, Shaowei Wan, Yu-Yu Tien, Cole Chapman, Matt Nattinger, Oscar Garza, Erin Thatcher, Yin Wan, Daniel Ashcroft, Yiran Zhang, Ziqian Chen, Yan Zhang, Ben Urick, Aaron Miller, Jacob Simmering, Chien-Hsun Li, and Ali Al Jumaili. A special thank you to Tamara Wilde, Beth Cook, and Lois Baker for helping me through big and small things in my graduate school.

My friends in the United States have also made my life so much easier and cheerful in Iowa City. Especially, Min Wang started graduate school the same year as me. We have been through a lot of laughs and complain in our girl's chat that helps with our mental health significantly in graduate school, while being so far away from family. Mariah Gerali, Earldean and Bill Miller have also made me feel home and family and turned my life in graduate school wonderful.

ABSTRACT

Observational data and alternative estimators with correct interpretations have been used to assess the "right" treatment rates in previous studies. However, no systematic analytical approach has been proposed to examine whether the existing diagnosis rates were right in practice. This study used patients with acute myocardial infarction (AMI) as an example to demonstrate use of observational data to explore the clinical and economic effects of depression diagnosis and the "right" depression diagnosis rates in real-world settings. The objectives of this study were to (1) examine the effects of depression diagnosing on survival, healthcare costs and utilization among elderly patients with AMI; and (2) ascertain bounds on the estimates of the effects of depression diagnosing on survival, healthcare costs and utilization based on chart abstracted data for a subset of patients.

Using Medicare claims data, we included a retrospective cohort of all Medicare fee-for-service patients with their first AMI without a depression diagnosis in the previous year during 2007-2008. Depression diagnosis was identified if a patient had a depression diagnosis within 30 days after AMI admission. We also assessed the effects of depression diagnosis within 60 and 90 days after AMI admission. Outcomes were survival, healthcare costs (total costs, Part A, Part B (outpatient, physician fee schedule, and other), and Part D costs), and utilization (hospitalizations, emergency department (ED) visits, outpatient visits, physician visits, and prescription claims) within 1 year after AMI admission. Risk adjustment (RA) and instrumental variables (IV) models were used to estimate the effects of depression diagnosis on AMI patient outcomes. Instruments of local area depression diagnosis styles were created based on area diagnosis ratio (ADR). Using chart abstracted data for a convenience sample, we measured patient physical functional status by difficulties with activities of daily living (ADL) and overall health by

adult comorbidity evaluation-27 (ACE-27), AMI severity, and mental illnesses during the index hospitalization.

Among 155841 AMI patients in our study sample, 5.9% had a depression diagnosis within 30 days after AMI admission. Our RA estimates showed that depression diagnosis was associated with decreased survival, increased total healthcare costs, Part A costs, Part B outpatient costs, hospitalizations, ED visits, physician visits, and prescription claims in 1 year after AMI admission for patients diagnosed with depression. The ADR-based instruments were strongly related to depression diagnosis (Chow-F values > 10). Our IV estimates showed that higher depression diagnosis rates were associated with increased total healthcare costs, Part A costs, Part B physician fee schedule costs, Part B other costs, Part D costs, and physician visits, but decreased ED visits and prescription claims in 1 year after AMI admission for patients whose depression diagnosis was affected by ADR-based instruments.

Since patients diagnosed with depression were more likely to be sicker based on measures in the charts, the RA estimates might be biased toward worse health outcomes and higher healthcare costs and utilization. Across patients grouped by local depression diagnosis styles, the measures in the charts were more evenly distributed across diagnosis groups. However, patients living in areas with stronger preferences of depression diagnosis tended to use more wheelchairs, indicating worse physical function than those living in areas with less stronger preferences. Furthermore, our instruments based on local physician depression diagnosis styles might be correlated with local area practice styles in general (preference to healthcare utilization overall) and local physician supply, and thereby affect healthcare utilization and costs. Therefore, the instruments might not be valid and we could not conclude whether the existing depression diagnosis rates need to be changed.

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CHAPTER I

INTRODUCTION

Depression is very common among adults in the United States. More than 1 in 5 adults in the United States experience depression during their lifetime[1] and almost 1 in 10 adults have had depression in the previous year.[2] In 2000, the economic burden of depression in the United States was estimated to be $83.1 billion, including $51.5 billion work-related costs, $26.1 billion direct medical costs, and $5.4 billion suicide-related mortality costs.[3] New evidence has drawn attention to the negative effects of depression on elder patient health, as well as its associated economic burden. Depression can increase healthcare costs,[4-8] the risk of cardiovascular disease,[9-24]suicide,[25, 26] mortality,[27-32] and disability,[33-35] while it can decrease quality of life[36] and physical function,[37] especially for older adults. Thus, it is imperative to recognize depression to provide optimal care in the elderly.[38-40]

Many mental illnesses, including depression, are treatable. It has been suggested that prompt diagnosis and treatment can help control symptoms and minimize dysfunction for patients with mental illnesses.[41-45] Diagnosing depression serves as the gateway for patients to receive appropriate depression treatments.[46] For elderly patients diagnosed with depression, treatments such as antidepressants and psychotherapy have been reported to be safe and efficacious.[39, 40, 47-51] However, in practice, it is thought by some that appropriate recognition and diagnosis of depression is poor, with many studies suggesting under-diagnosing of depression in the elderly.[39, 43, 49, 52-61] The National Institutes of Health Consensus Panel stated that under-diagnosing of depression represents a major problem in the elderly, particularly in those with physical illnesses, and suggested that depression is more prevalent than is currently diagnosed.[39, 62]

However, other studies have raised concerns about over-diagnosis and misdiagnosis of depression.[63-67] If depression is currently over diagnosed, higher depression diagnosis rates may not lead to better outcomes. Also, depression can vary in

severity.[68] Meta-analyses combining data from several randomized controlled trials (RCTs) demonstrated that the benefits of antidepressants are substantial for patients with more severe depressive symptoms, whereas the benefits are minimal for patients with mild or moderate depression.[69, 70] This heterogeneous effect is also found for psychotherapy with substantial benefits for patients with severe depression, but not for those with mild or moderate depression.[71-73] In addition, many studies have shown that patients with the most severe symptoms of depression are the most likely to receive a diagnosis of depression.[45, 53, 56, 59, 74-80] Therefore, if providers believe the benefits of depression treatments vary across patients, and in practice they are sorting patients based on these beliefs, then, on average, presently diagnosed patients should have more severe depression than undiagnosed depressed patients. This type of sorting has been described as *essential heterogeneity*, where expected treatment effectiveness varies across patients and provider treatment decisions reflect these different expectations, i.e. sorting on the gain.[81] Essential heterogeneity may be consistent with the notion of patient-centered care where healthcare is provided to patients based upon the treatment benefits expected for each patient given individual characteristics and preferences.[82, 83] If depression diagnosing is currently correctly sorted across patients, higher depression diagnosis rates would lead to patients with less severe depression receiving a diagnosis of depression with little to be gained from the treatment that follows diagnosis.

Are providers sorting depressed patients correctly based on these beliefs, or is depression under-diagnosed as many studies suggest?[39, 43, 49, 52-59, 61] The real question, therefore, is "which rate is right"-- posed by John Wennberg over two decades ago.[84] There are three possible answers to Wennberg's question with regard to current depression diagnosis rates. First, if depression treatments are effective only for currently diagnosed patients, the current sorting is right and expanding depression diagnosis rates would add little value for the undiagnosed patients. Second, if undiagnosed patients with depression could benefit from depression treatment, the current sorting is wrong and

current depression diagnosis rates should be expanded. Third, if depression treatments are not effective for some currently diagnosed patients, the current sorting is wrong and depression is currently over-diagnosed.

How do we answer Wennberg's question? First, we need to find a source of variation in depression diagnosing across patients in current practice to exploit for analysis. Second, outcomes need to be compared from variation in depression diagnosing. Previous research on depression recognition primarily used an approach to examine depression diagnosis discordance that compared depression diagnoses by physicians with diagnostic criteria based on structured interview or questionnaires for a small sample of patients in healthcare settings.[52-57, 59-61] However, the criteria used to determine depression diagnosis varied substantially across these studies, which may not represent depression diagnostic criteria adopted by physicians in real-world settings. Furthermore, studies using this method did not evaluate outcomes following depression recognition (e.g. quality of life, survival, healthcare utilization, and costs). Understanding whether *additional diagnosis* has value is key to answering Wennberg's question in this context. Especially given depression treatment-effect heterogeneity that patients with more severe depression benefit more from depression treatments, it is possible that additional depression diagnosing will provide little or no benefits for the newly diagnosed patients with less severe depression. Thus, it is unclear if depression is truly under-diagnosed as claimed by the National Institutes of Health Consensus Panel.

RCTs generate treatment variation through random assignment and are considered to be the gold standard for clinical research. Unfortunately, the random assignment of patients to diagnoses appears unethical.[85] It may be possible to randomly assign patients to depression screening programs. Thus, patients assigned to the screening group are more likely to receive a depression diagnosis than those assigned to the usual care group. While this may be ethical, it would only be possible to include a small number of patients in studies of this type, which would limit the ability to generalize study results to a larger

population. Prior to conducting expensive and time-consuming RCTs, other study designs are available to provide a first step in understanding whether depression is under or over-diagnosed in practice.

Another approach is to try to exploit the variation in depression diagnosing found in observational data.[85, 86] Use of observational data enables analysis of real world physician depression diagnosing choices. Furthermore, use of observational data enables researchers to investigate outcomes following depression diagnosing and to identify heterogeneous effects with a large number of patients in practice. Thus, this study assessed whether depression is currently over- or under-diagnosed in practice using observational data as a first step in addressing Wennberg's question in this important context.

Our analytical approach to estimate the effects of diagnosing depression using observational data included both risk adjustment (RA) and instrumental variable (IV) estimators that yield average effect estimates for different subsets of the population. RA estimators provide estimates of the average treatment effects for the treated.[87, 88] With the focus of this research being depression diagnosing, RA estimators yielded the average effects of diagnosing depression for patients who received a depression diagnosis. An RA estimator yields unbiased estimates of the effect of diagnosing depression on the diagnosed if unmeasured factors affecting outcomes, such as disease severity, are unrelated to the diagnosing decisions.[89-91] IV estimators provide an estimate of the local average treatment effect for marginal patients. Marginal patients have been defined in the IV literature as those patients whose treatment choices were affected by "instruments".[92] A valid "instrument" is a measured factor that is strongly related to treatment decision, but unrelated to unmeasured factors affecting outcomes.[93] In this research, IV estimators yielded average effects of depression diagnosing for patients whose depression diagnosis was affected by the instruments specified.[87, 88] It has been suggested that practice styles across local areas can be used as instruments in research to explore over/underuse of

medical care.[94-98] That is, local "schools of thought," where physicians hold different beliefs about treatment effects, lead to variation in practice styles on regional or community levels.[99] We developed a model using measures of the local area depression diagnosing styles as instruments. The model was checked for robustness by using other measures as instruments.

In this study, we used RA and IV estimates with observational data to investigate whether existing depression diagnosis rates were "right". We focused on a population for whom depression rates are thought to be high.[100-102] and studies have identified pathological and behavioral mechanisms to explain the association between depression and cardiac prognoses.[103-106] Given the high depression rates among AMI patients and suggested linkage of depression to worsening cardiovascular outcomes, depression is frequently reported to be underdiagnosed or undertreated.[107-112] Again, these studies did not evaluate outcomes associated with depression diagnosis and only included a small sample. Therefore, little evidence exists on whether current patterns of diagnosing depression in this population are suboptimal. This dissertation used a retrospective cohort of Medicare beneficiaries hospitalized with AMI to evaluate depression diagnosing effects to help address the question of whether depression is currently over- or under-diagnosed. The following specific aims were pursued:

Aim 1: Examine the effects of depression diagnosing on survival, healthcare costs and utilization among elderly patients with AMI.

Given the widely-reported under-diagnosis of depression among AMI patients,[107-112] the null hypothesis is that the current depression diagnosis rate is wrong and expanding the depression diagnosis rate would lead to higher survival and lower healthcare costs and utilization.

Aim 2: Ascertain bounds on the estimates of the effects of depression diagnosing on survival, healthcare costs and utilization based on chart abstracted data for a subset of patients.

Under the null hypothesis that RA assumptions are true, then the confounders measured in the charts but unmeasured in Medicare claims data are evenly distributed across depression diagnosis groups. Under the null hypothesis that IV assumptions are true, then the confounders are evenly distributed across patients grouped by local area depression diagnosing styles. We used both RA and IV estimates in Aim 1 with information on bias directions from Aim 2 and shed light on the "right rate" of diagnosis.

This proposed study is innovative because we evaluated whether the existing diagnosis rates were "right" using alternative estimators with correct interpretations using observational data. This systematic analytical approach has been used in assessing the "right" treatment rates in health economics literature, but not in answering "which rate is right" for diagnosis.[87, 88, 94-96, 113-118] This study design using observational data provides useful information to clinicians on over-/under-diagnosis issues in practice. More importantly, study findings could be used to assist policy makers in examining whether changes in diagnosis rates are warranted to improve survival and reduce healthcare expenditures and utilization. Knowledge gaps relating to the effects of diagnosis in real-world practice can never be fully addressed using RCTs alone. This study used AMI patients as an example to demonstrate use of observational data to explore the clinical and economic effects of diagnosing depression and the "right" depression diagnosis rates.

CHAPTER II

LITERATURE REVIEW

Overview

This literature review is organized as follows: first, the importance of diagnosing depression in practice is summarized. Second, factors that have been shown to affect diagnosing depression are discussed. Third, depression treatment-effect heterogeneity is presented to introduce the "which rate is right" debate with regards to whether depression is currently over- or under-diagnosed. Fourth, alternative estimators used in observational studies, such as risk adjustment and instrumental variables estimators, are discussed to illustrate the analytical approach applied in this dissertation and to explain why this method can contribute to the knowledge gap of the over/under diagnosing problem regarding depression.

Importance of diagnosing depression

Depression represents a common and significant healthcare problem with increased healthcare costs and negative health consequences in the United States. It is thought that more than 1 in 5 adults in the United States experience depression during their lifetime[1] and almost 1 in 10 adults have had depression in the previous 12 months.[2] Major depressive disorder (MDD) as a long-lasting and severe form of depression occurs in more than 1 in 7 adults in the United States during their lifetime[1] and 1 in 15 adults have had MDD in the previous 12 months.[2] Among patients with MDD in the previous 12 months, 20% have experienced mild depressive symptoms, 50% have experienced moderate depressive symptoms, and 30% have experienced severe depressive symptoms.[2] Between 1990 and 2000, the economic burden associated with depression in the United States increased by 7%.[3] Of the $83.1 billion total costs in 2000, $51.5 billion was work-related, $26.1 billion was direct medical costs, and $5.4 billion was suicide-related mortality costs.[3]

In the past two decades, research has drawn increasing attention to the negative consequences of depression on healthcare costs and patient health. Patients with depression had significantly higher total healthcare costs than those without.[4, 6-8] Beyond higher depression treatment-related costs,[4, 6] patients with depression had increased costs for other medical conditions[4, 6] and out-of-pocket healthcare expenditures[8]. In addition, mounting evidence has revealed that depression is associated with increased risk of cardiovascular diseases,[9-24] especially in the elderly. Meta-analyses and systematic reviews support a dose-response relationship between depression and cardiovascular disease in which more severe depression is related to worsening cardiac outcomes.[119, 120] Depression has also been shown to increase the risk of suicide,[25, 26] mortality,[27-32] and disability,[33-35] while it can decrease quality of life[36] and physical function[37] for older adults. Thus, it is critical to diagnose and treat depression in the elderly population to improve patient health and control healthcare costs.[38-40]

It has been suggested that if promptly diagnosed, many mental illnesses, including depression, are treatable.[41-45] Over 30 years ago, Butler first suggested that the elderly have not been provided with the level of psychiatric treatment, services, and research commensurate with their needs, especially given that the elderly are disproportionately susceptible to mental problems.[41, 42] Still, normal aging with changes in intellectual and physical function in the elderly does not include depression or other mental illnesses.[41, 42] Instead, such depressive symptoms result from disease processes and require professional diagnosis and treatment.[41, 42] Previous studies have shown that depression treatments are safe and efficacious for the elderly diagnosed with depression.[39, 40, 47-51] Two classes of antidepressants, selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are both considered first-line treatment strategies for depression in the elderly.[121, 122] The efficacy of psychotherapy for depression was also supported among older adults, especially for long-term treatment strategies, for those who cannot tolerate antidepressants, or for those who are facing

interpersonal difficulties, low levels of social support, or obviously stressful situations.[39, 40, 49-51] However, in a 10-year-old national questionnaire study that investigated general practitioners' attitudes toward depression management, general practitioners thought "depression is very difficult to treat in the elderly", primarily because older adults show atypical depressive symptoms and some symptoms were masked by other medical conditions.[44]

High depression prevalence rates have been frequently reported in the elderly. It has been estimated that 17% of seniors in communities[123-126] and 29% in primary care settings[74, 75, 127] have depression. Among hospitalized older adults, estimated MDD rates vary from 10% to 45%, and rates of minor depression range from 8% to 25%.[53, 128, 129] Diagnosing depression serves as the gateway for patients with depression to receive appropriate treatments.[46] Since studies focusing on depression diagnosis in practice is limited, this literature review expanded searching to depression recognition that includes depression diagnosis, antidepressant use, referral to a specialist for psychiatric consultation[43, 52-54, 56, 60], and questions asked to physicians about whether a patient has depression[55, 57]. Studies have reported that depression recognition was associated with better health and economic outcomes even in a short term (within 1-year after intervention), such as improved depressive symptoms[130-135], decreased hospitalizations/ED visits[131, 136-138], improved patient satisfaction/adherence to the treatment plan and quality of mental health[130, 132], quality of life[139], adherence to aspirin[140], and decreased healthcare costs[135, 139, 141].

However, in practice, appropriate diagnosis of depression is thought to be poor and depression is frequently incorrectly diagnosed.[39, 43, 49, 52-61] Many studies have suggested that under-diagnosis of depression represents a major problem in the elderly.[39, 43, 49, 52-61] In a study of 264 hospitalized adults aged 65 years and older in Canada, less than half of depressed patients were recognized as depressed by their attending physicians based on the Diagnostic Interview Schedule.[53] A systematic review and meta-

analysis revealed that depression recognition by non-psychiatrist physicians suffers from low accuracy.[43] This evaluation showed that about 40% of patients of all ages with depression were recognized by non-psychiatrist physicians, while only 30% of elderly depressed patients were recognized. Furthermore, the authors found considerable variability in criteria measures and recognition methods for depression across individual studies in the systematic review and meta-analysis. These individual studies used either a structured clinical interview or a rating scale with a cut point as depression diagnostic criteria. Given the lack of standardized methods of documenting physicians' recognition of depression in the literature, caution should be taken when interpreting depression recognition rates.

As early as the 1990s, the National Institutes of Health Consensus Panel stated that the under-diagnosing of depression represents a major problem in the elderly, particularly for those with physical illnesses, and suggested that depression is more prevalent than is currently diagnosed.[39, 62] However, the statement did not provide specific references to support the under-diagnosis of depression in the elderly on a population level. Empirical studies published before the National Institutes of Health Consensus Panel statement showed depression was under-diagnosed in a specific healthcare setting using only a small sample of patients and different diagnostic criteria (structured interviews or questionnaires) to determine whether a patient had depression.[60, 61]

In the medical literature, diagnosing depression has been widely discussed with a variety of study designs demonstrating under-diagnosis or under-recognition problems. However, these previous studies contained small numbers of patients and were focused in specific healthcare settings that limit the ability to generalize study results to the general population. Additionally, several different approaches to recognize depression exist, including depression diagnosis alone,[59, 61] depression diagnosis, treatments, and psychiatric referral[43, 52-56, 60], and questions asked to physicians about whether a patient

has depression[55, 57]. As a result, patients with only a psychiatric referral may be recognized in studies using a broader definition of depression recognition, while they may not be recognized in studies using depression diagnosis alone as recognition measure. Furthermore, criteria used to determine a patient's underlying depression are based on structured interviews[53, 55, 59] or questionnaires.[52, 54-57, 59] It is possible that some patients who were assessed as depressed using depression rating scale questionnaires might not be considered depressed using structured interviews. With these various study designs in previous studies on sample selection, depression recognition measures, and depression criteria measures, substantial variation in depression recognition rates exists ranging from 9.5% to 42.6% among depressed patients.[52-57, 59] Furthermore, if depression treatment effects vary across patients[69-73] and physicians make diagnosing decisions based on treatment-effect heterogeneity, it is impossible to determine the "right rate" with a small sample of patients who may not represent the general population in the real world. Lastly, no studies have assessed outcomes following depression diagnosis in practice (e.g. survival, healthcare utilization, cost, and quality of life), which are key to determining whether depression is currently over- or under-diagnosed.

Compared to the widely-reported under-diagnosis of depression, a few studies have raised concerns about over-diagnosing and misdiagnosing depression.[64-67, 142, 143] Among patients diagnosed with depression in hospitals and primary care settings, 40% to 50% did not meet the criteria fordepression.[53, 64, 65, 143] It has been argued that over-diagnosing depression can lead to unnecessary and ineffective treatments.[66, 67] If depression is currently over-diagnosed, higher depression diagnosis rates may not lead to better outcomes. With the mixed evidence on depression diagnosis, it is still not clear whether depression is over- or under-diagnosed in practice. This research would shed light on the right depression diagnosis rates.

Factors affecting depression diagnosing decisions

Diagnosing depression is a complex decision that involves physicians recognizing patient depressive symptoms and making a correct diagnosis after interacting with patients.[68] To assess the effectiveness of diagnosing depression, it is necessary to understand factors affecting diagnosing decisions. First of all, we need to understand what depression is. According to the National Institute of Mental Health, there are several forms of depression, including MDD, dysthymia, and minor depression.[68] MDD is severe and long-lasting depression that is disabling and prevents patients from normal functioning.[68] From the most accepted standard to assess depression, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines MDD as an individual experiencing at least five of the following symptoms nearly every day during the same 2-week period: depressed mood, diminished interest, weight change, sleep change, psychomotor agitation or retardation, loss of energy, feelings of guilt, diminished ability to concentrate, and thoughts of suicide.[144] Either depressed mood or diminished interest must be present as one of the symptoms to diagnose MDD.[144] Older adults may not present with typical depressive symptoms as listed in the DSM criteria.[145] Instead, atypical presentation of depressive symptoms in seniors with depression include denying sadness or depressed mood, unexplained somatic complaints, hopelessness, helplessness, anxiety, worries, memory complaints, anhedonia, slowed movement, irritability, and general lack of interest in personal care.[145] Dysthymia is long term depression that can prevent patients from normal functioning or feeling well, but may not be disabling.[68] Patients who do not meet full criteria for major depression but experience depressive symptoms lasting two weeks or longer have minor depression.[68] Patients with minor depression would be at high risk of MDD without treatment, even though patients with minor depression do not have symptoms as severe as those with MDD.[68] These differences in depressive symptoms are associated with depression severity and are potential sources of variation in depression diagnosing decisions.

To understand factors affecting depression diagnosing decision, it is important to distinguish factors associated with underling depression severity and those associated with physician's beliefs about depression diagnosis and treatment benefits. A model of physician decision to diagnose depression was developed in the theory section to illustrate how these factors affect depression diagnosing decision.

Factors affecting depression diagnosing decision via underlying depression severity include patient physical function, overall health, and contextual factors. Patients with poor overall health are more likely to have severe depressive symptoms and to be diagnosed with depression,[6, 53, 79] while those with more physical function are less likely to have severe depressive symptoms and to be diagnosed with depression.[60, 76, 80] People living in areas with low temperature and lack of sunlight are more likely to have severe depressive symptoms, which therefore affects depression diagnosis.[146] Besides environmental factors, other contextual factors affecting depression severity include urban living and neighborhood characteristics.[147, 148] Romans et al. demonstrated that people living in rural areas were less likely to have severe depressive symptoms than those in urban areas.[148] A review study showed that people living in the neighborhood with socioeconomic disadvantage (e.g. income and education), high poverty, many problems (e.g. crime rate), and high walkability are more likely to develop severe depressive symptoms and to be diagnosed with depression.[147]In contrast, high residential mobility (e.g. percentage of residents in the neighborhood who have lived in their household for less than five years) has been frequently reported to be associated with low probability of having severe depression.[147]

Besides factors affecting underlying depression, some factors can also influence depression diagnosing decision through physician's beliefs in the benefits of depression diagnosis. Variation in diagnosing depression can come from different approaches that physicians adopt to detect and manage depression in the local healthcare system.[149] The lack of a gold standard for assessing and managing depression in the real world leaves

immense discretion to physicians in diagnosing depression.[46] Without a gold standard, it is almost infeasible for physicians to develop a consistent approach to managing depression in the local healthcare system. In this case, physicians may not believe that diagnosing depression is beneficial due to lack of a systematic approach to detecting and managing depression.

Factors affecting the depression diagnosing decision through physician's beliefs in the benefits of depression diagnosis can stem from patients. Accurately diagnosing depression depends on patients' ability to communicate with healthcare providers about depressive symptoms.[150-154] For example, patients may not fully articulate depressive symptoms with healthcare providers. Patients have been reported to be uncomfortable discussing mental health problems with healthcare providers due to concerns about stigmas associated with mental health issues.[150, 151] Patients may lack knowledge and ability to recognize or report depressive symptoms.[152] In addition, depression diagnosing decisions depend on a patient's willingness to accept a depression diagnosis.[150, 152-154] Patients may also deny a depression diagnosis as a result of perceived disapproval from family and friends [150]or attribute symptoms of depression to medical conditions other than depression.[153, 154] These patient-related factors could affect physician-patient interactions during depression assessment. These interactions, in turn, can influence physicians' beliefs about benefits of depression diagnosis and its following treatments for individual patients.

Factors affecting depression diagnosing decision through physician's beliefs in the benefits of depression diagnosis can come from physicians. Physician "deficits" in the understanding of the disease and its treatments may affect physician's beliefs in the benefits of depression diagnosis.[46, 151, 155-159] Some physicians believe that depression is a normal reaction with advanced age or that it reflects personal laziness that the patient could improve with more willpower or positive thinking.[46, 151, 159] Some physicians may be more comfortable assessing physical rather than psychological complaints, often due

to stigmas of mental illnesses.[46, 155-158] This appears to be the case especially for the elderly.[46] Others have doubted depression as a clinical entity due to lack of confirmatory laboratory or radiologic studies.[46, 151] These physician-related factors could affect physicians' beliefs in the benefits of depression diagnosis and its following treatments on health outcomes, which in turn affect a physician's decision to diagnose depression.

Even if physicians consider depression as a clinical entity, lack of ability and knowledge of diagnosing depression may affect their diagnosing decision through beliefs in the benefits of depression diagnosis.[46, 155, 160] Without adopting effective interviewing techniques, physicians may prevent patients from talking effectively about uncomfortable psychosocial material.[46, 155] Some physicians may not recognize nonverbal cues or ask questions corresponding to indications of distress, thus preventing discussion of mental health problems from ocurring.[46] Failure to offer support and empathy during the interview could be interpreted by patients as a physician's unwillingness to discuss mental health concerns,[46] and affect physician-patient interactions during depression assessment.

Previous research has also reported that some patient characteristics affect depression diagnosing decision. Patient demographics could influence depression diagnosing decisions through physician expected patient health. Males,[6, 79, 161-163] younger patients,[6, 162, 163] and minorities[52, 161, 162] are less likely to be diagnosed with depression, while some studies showed younger patients are more likely to be diagnosed with depression.[45, 75] In addition, patients' medical conditions and healthcare resource use have been identified as factors affecting depression diagnosing decisions. For example, patients with less severe depressive symptoms,[45, 53, 56, 59, 74-80] no prior antidepressant use,[53, 75] or no history of depression[53, 56, 164] are less likely to be diagnosed with depression. However, study findings on psychiatric comorbidities are mixed.[6, 59, 74, 76, 80] Patients without disabilities[164] and cardiovascular disease[52, 56, 161] are less likely to be

diagnosed with depression. Nevertheless, patients with less comorbidity are more likely to be diagnosed.[53]

In the theory section, we developed a model of physician decision to diagnose depression. The model included factors affecting depression diagnosing decision in prior research and demonstrated how they are theorized to affect diagnosing decision.

Depression treatment-effect heterogeneity

Depression treatment effects vary across patients. Meta-analyses of randomized controlled trials have demonstrated that the benefits of antidepressant use increase with severity of depressive symptoms.[69, 70] One of two meta-analyses demonstrated that the benefits of antidepressants compared with placebo are shown to be minimal for patients with mild or moderate MDD, whereas the improvements in depressive symptoms from antidepressants are substantial for patients with the most severe MDD.[70] The other meta-analysis found consistent evidence on treatment-effect heterogeneity for patients with MDD and minor depression.[69] Previous studies have also shown that the benefits of psychotherapy are substantial for patients with severe depression but minimal for those with mild or moderate depression, including both MDD and minor depression.[71-73] However, depression severity was measured by different rating scales, including the Depression Symptom Checklist[71-73] and the Hamilton Depression Rating Scale.[69, 70] Lacking of a consistent measure of depression severity, depression categorized to be severe in one rating scale may not be considered severe in another, which may affect study results of depression treatment-effect heterogeneity that rely on depression severity measures.

Not everyone with depressive symptoms receives a depression diagnosis. An international longitudinal study reported only 42% of depressed patients aged 65 and younger were recognized by their primary care physicians with a depression diagnosis. Research has further shown that patients with more severe depressive symptoms are more likely to receive a diagnosis of depression.[45, 53, 56, 59, 74-80] Among patients with physician-

diagnosed depression, 46% had severe, 34% had moderate, and only 2% had mild depressive episodes; among those undiagnosed patients with depression, 25% had severe, 41% had moderate, and 34% had mild depression.[45] Simmon et al. also showed that diagnosing depression was associated with significant short-term improvements in depressive symptoms.[45] Furthermore, their study suggested that effects of diagnosing depression on short-term symptom improvement might be greatest in patients with the most severe depressive symptoms.[45] In this international longitudinal study, physicians were asked to give a diagnosis and to rate patient depressive symptoms, which may not reflect the real-world practice of diagnosing depression.[45] Moreover, the authors acknowledged that the effects of diagnosing depression on symptom improvements might be biased toward null due to incomplete adjustment for patient baseline characteristics and the nature of non-randomized assignment, in which physicians tend to recognize patients with more severe depression and greater functional impairment.[45]

Depression severity is essential in assessing the issue of under- or over-diagnosis of depression in practice. Prior research has reported that depression severity affects depression treatment effects and that the effects increase with depression severity.[69-73] Simmon et al. also reported that the effects of depression diagnosis increase with depression severity.[45] Their study measured depression severity using the Composite International Diagnostic Interview.[45] However, with different measures of depression severity in previous studies,[45, 69-73] it can be problematic to interpret findings across studies and to draw a conclusion on the effects of depression diagnosing. Therefore, research is needed to assess the effects of diagnosing depression using an unbiased estimator and to examine whether depression is currently under-diagnosed in practice. We developed a model of physician decision to diagnose depression in the theory section and illustrate how depression severity affects diagnosing decisions, given heterogeneous depression treatment effects.[69-73]

Estimate interpretation under treatment-effect heterogeneity

Treatment-effect heterogeneity, or the idea that treatment effects vary across patients with a given condition, is well-established in healthcare.[87, 88, 165-167] Attempts to discuss "average effects" from one study population can become misleading as individual patients might depart significantly from the population average.[165] As a result, applying the average effects of treatments in clinical trials to individual patients may not be appropriate. If providers believe treatment benefits vary across patients, and in practice they sort patients based on these beliefs, then, on average, treated patients should have higher treatment benefits than the untreated. This type of sorting has been described as *essential heterogeneity,* where expected treatment effectiveness varies across patients and provider treatment decisions reflect these expected differences, i.e. sorting on the gain.[81] In this research, the treatment is diagnosing depression. If physicians believe depression treatment effects vary across patients and sort patients based on these beliefs correctly, then, on average, currently diagnosed patients should have higher benefits from a depression diagnosis and its following treatments than the undiagnosed. In this case, increasing depression diagnosis rates would lead to patients receiving a diagnosis with less to be gained from its following treatments than those already diagnosed.

Are providers sorting depressed patients correctly in practice based on beliefs about heterogeneous effects of diagnosis across patients, or is depression under-diagnosed as many studies suggest?[39, 43, 49, 52-59, 61] The real question, therefore, is "which rate is right?"-- posed by John Wennberg over two decades ago.[84] Figure 2.1a gives a graphical example of three possible answers to Wennberg's question with regard to depression diagnosis rates. The solid-red line represents the true benefit of depression diagnosis in health production function, with patients ordered from the highest to the lowest treatment benefit moving from left to right on the horizontal axis. Health production function was fully discussed in the theory section later. An example of depression treatment benefits is survival benefit associated with depression diagnosis and

its subsequent treatments. The solid-green line represents the true cost of depression diagnosis and its following treatment. For simplicity, we assume constant treatment cost in this example. The net treatment benefit is calculated by treatment benefit minus cost. Given the heterogeneity of depression treatment effects across patients shown in the graph, patients with the greatest treatment benefits relative to treatment costs are those with the most severe depression, who are the most likely to be diagnosed with depression, whereas patients with the least treatment benefits relative to treatment costs are those with the least severe depression, who are the least likely to be diagnosed. As shown in Figure 2.1a, patients are sorted from the highest to lowest treatment benefits relative to treatment costs from left to right on the X-axis, which also represents a patient's decreasing probability of receiving a depression diagnosis. P is the optimal diagnosis rate where the benefit of depression diagnosis equals its cost.

However, in practice, given the dearth of firm evidence supporting depression diagnosing decisions, plenty of discretion is involved and many factors can affect this decision that can lead to rates differing from P. A model of physician decision to diagnose depression was fully discussed with factors affecting the decision in the theory section. For example, physician beliefs about depression treatment benefits may affect depression diagnosing decisions through expected patient health. If physician's beliefs about depression treatment benefits are the same as true depression treatment benefits, depression diagnosis rate is P. In this case, depression treatments are effective only for currently diagnosed patients, the sorting is correct, and expanding depression diagnosis rates would add little value for the undiagnosed patients. At this rate, P, all diagnosed patients (P) benefit from depression treatments and all undiagnosed patients (1 – P)would not have benefited from depression treatment.

If a physician's belief about depression treatment benefits is smaller than the true depression treatment benefits, depression diagnosis rate is P_1 (Figure 2.1b**)**. A dashed-black line represents an underestimate of treatment benefits. In this case, all diagnosed

patients and some undiagnosed patients ($P - P_1$) benefit from depression treatment and other undiagnosed ($1 – P$) patients would not have benefited from depression treatment. The sorting is incorrect and the depression diagnosis rate (P_1) should be expanded.

If physician's belief about depression treatment benefits is greater than the true depression treatment benefits, the depression diagnosis rate is P_2 (Figure 2.1c**)**. The dashed-black line represents an overestimate of treatment benefits. At this rate, P_2, some diagnosed patients benefit from depression treatment and other diagnosed patients ($P_2 – P$) and all undiagnosed patients ($1 – P_2$) would not benefit from depression treatment. The sorting is incorrect and depression is over-diagnosed.

Estimators in observational studies

To answer Wennberg's question regarding the "right rate", sources of variation in depression diagnosis rates are needed to be exploited for analytical purposes and outcome comparison associated with this variation. Observational data have been suggested as a source of treatment variation that could be used to compare outcomes resulting from treatment variation.[85, 86] Use of observational data may enable researchers to estimate average treatment effects for different subsets of the population given treatment-effect heterogeneity.[85, 86] Use of observational data with a large sample may also ensure generalizing average treatment effects to the general population.[85, 86] In this study, to assess the effects of diagnosing depression on health outcomes, we adopted an analytical approach using both risk adjustment (RA) and instrumental variables (IV) estimators with observational data. RA and IV estimators yield average effect estimates for different subsets of the population.[87, 88] RA estimators yield average treatment effects on the treated (ATT) and IV estimators yield estimates of local average treatment effects for patients whose treatment choice is affected by instruments (LATE).[81, 87, 88, 92, 118, 168-177]

If treatment benefits vary across patients in practice and treatment choice is made based on the expected treatment benefits, the treated patients (framed by the green box in Figure 2.2**;** darker color represents greater treatment benefits) are expected to benefit

more from the treatment than the untreated. Given essential heterogeneity, estimates of ATT cannot identify the average treatment effect across the population (ATE) or the average treatment effect on the untreated (ATU). Given depression treatment-effect heterogeneity,[45, 69-73] if physicians sort patients and make depression diagnosing decisions based on beliefs of treatment effect-heterogeneity, RA estimators yield the average effects of depression diagnosing for patients who actually received a depression diagnosis. An unbiased RA estimate requires that unmeasured factors affecting outcomes, such as depression severity, are unrelated to the diagnosing decisions.[89-91]

In IV analysis, a "valid" instrument is a measured factor that is strongly related to treatment, but unrelated to unmeasured confounders.[93] To illustrate how IV estimators work, assume that a valid instrument can be measured (e.g. local area depression diagnosing preferences) and used to divide patients into two groups (Group 1 and Group 2 on the bottom of Figure 2.2). Patients of Group 2 residing in an area with stronger preferences for diagnosing depression would have a higher depression diagnosis rate than those of Group 1. Therefore, IV estimators identify a set of patients whose diagnosis is affected by the instruments due to relative small gain or loss from diagnosing depression, as depicted between the "Low" and "High" points in Figure 2.2. Patients with very high benefits of depression diagnosing from the diagnosis and its following treatments (e.g. patients above the "High" point) are expected to receive depression diagnoses regardless of the instrument groups. Likewise, patients with very few benefits are not expected to receive depression diagnoses regardless of the instrument groups (e.g. patients below "Low" point). Therefore, IV estimators yield the average effects of diagnosing depression only for those patients with the least extreme benefits and modifiable diagnosing decisions (e.g. patients between "Low" and "High" points).

How IV estimators work could also be demonstrated in Figure 2.3a-c based upon physician beliefs about depression treatment effects. In Figure 2.3a, when the depression diagnosis rate is P, the optimal depression diagnosis rate, RA estimators yield average

effects of depression diagnosis on the diagnosed (P%). IV estimators yield local average effects of depression diagnosis (values of benefit between B_L and B_H) on those whose diagnosis is affected by instruments due to relative small gain or loss from diagnosing depression (between P_L and P_H).If physician's beliefs about depression treatment benefits are smaller than the true depression treatment benefits, depression diagnosis rate is P_1 (Figure 2.3b**).** RA estimators yield average effects of depression diagnosis on the diagnosed (P_1%), while IV estimators yield average effects of diagnosing depression (values of benefit between B_{1L} and B_{1H}) for the patients between P_{1L} and P_{1H}.Ifphysician's beliefs about depression treatment benefits are greater than the true depression treatment benefits, depression diagnosis rate is P_2 (Figure 2.3c**).** RA estimators yield average effects of depression diagnosis on the diagnosed (P_2%), while IV estimators yield average effects of diagnosing depression (values of benefit between B_{2L} and B_{2H}) for the patients between P_{2L} and $P_{2H.}$

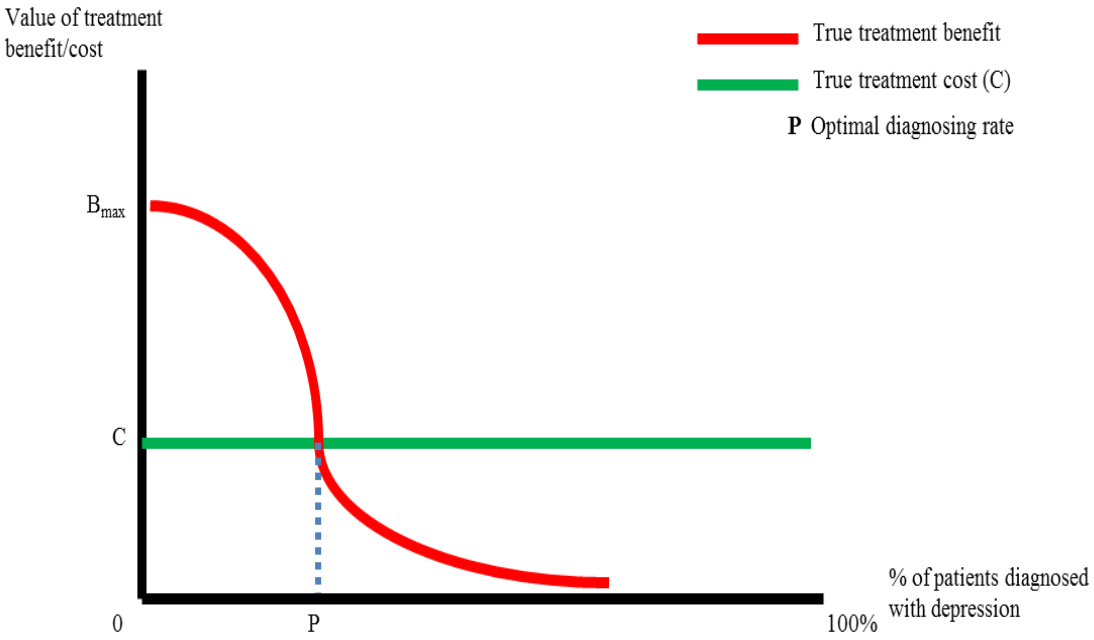
The next step is to find a valid instrument that meets the two requirements, is strongly related to treatment, but is unrelated to unmeasured confounders.[93]It has been suggested that geographic variation in physician practice styles can be used to develop instruments in IV estimation.[94-96, 98]A series of annual reports by Dartmouth have primarily focused on treatment practice style variation across local areas,[178] such as surgical procedures, but research on practice patterns of diagnosis is limited. In this dissertation, we developed a model using measures of local area depression diagnosis styles as instruments. The model was checked for robustness by using other measures (individual physician practice styles of depression diagnosis measured by prior depression diagnosis rates for each physician) as instruments.

In this study, we focused on a population where depression rates are high and controversial problems exist on diagnosing depression. Depression is a very common problem among patients that have had an acute myocardial infarction (AMI). More than half of patients with AMI experience depressive symptoms and 20% have MDD.[100-102] In

addition, review studies and meta-analyses have recently shown that depression is an independent risk factor of cardiovascular disease for patients with cardiovascular disease.[120, 179-185] Two principle mechanisms have been suggested to be responsible for the association between depression and cardiac prognosis, including behavioral and pathological pathways.[103-106] First, patients with depression tend to have lower adherence to recommended treatments or healthy lifestyle changes, such as exercise and smoking cessation, which leads to increased risk of cardiovascular disease. Second, the pathological pathways linking depression and prognosis of cardiovascular disease include dysregulation of the autonomic nervous system, platelet activation and endothelial dysfunction, hypothalamic-pituitary-adrenocortical and sympathetic adrenal medullary activation, inflammatory markers, and genetic polymorphism in the serotonin transport promoter region gene. Given the clinical and epidemiological evidence on the association between depression and cardiac prognosis, both the American College of Cardiology/American Heart Association (ACC/AHA) and the American Academy of Family Physicians (AAFP) guidelines recommend screening for depression during the post-AMI period, including during hospitalization.[186, 187]

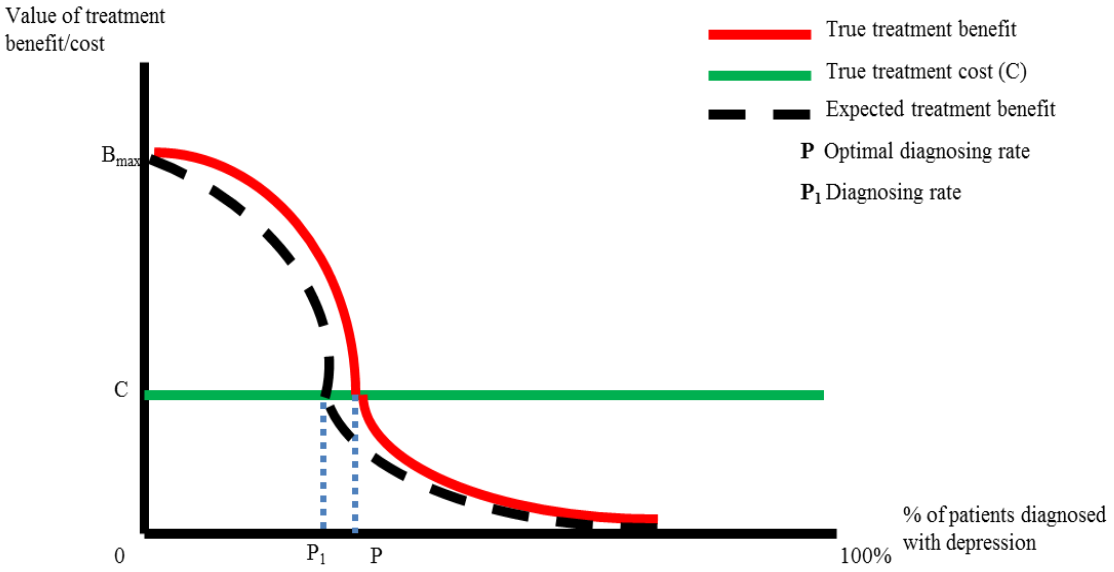
Diagnosing depression can serve as an important first step for depressed patients to initiate depression treatment with psychotherapy, antidepressants, or a combination of the two to improve health. Still, many studies reported depression was under-diagnosed/treated among AMI patients.[107-112] No studies have assessed the current patterns of diagnosing depression in practice and how diagnosing depression affects health outcomes in the AMI population. This dissertation used a retrospective cohort of Medicare beneficiaries hospitalized with AMI as an example to examine the effects of diagnosing depression on healthcare costs and survival. Furthermore, alternative estimators were used with correct interpretations to evaluate whether depression is over- or under-diagnosed in practice.

Figure 2.1. Graphical example of depression treatment-effect heterogeneity and depression diagnosing rates



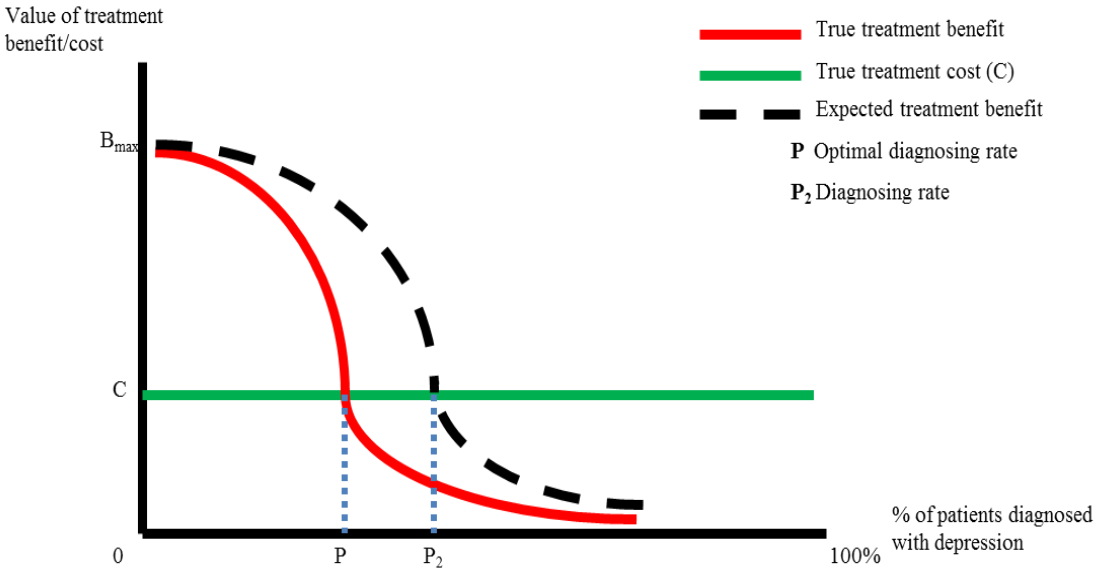
a. Correct estimate

Figure 2.1. Continued



b. Underestimate

Figure 2.1. Continued.



c. Overestimate

Figure 2.2. Graphical example of analytical approaches

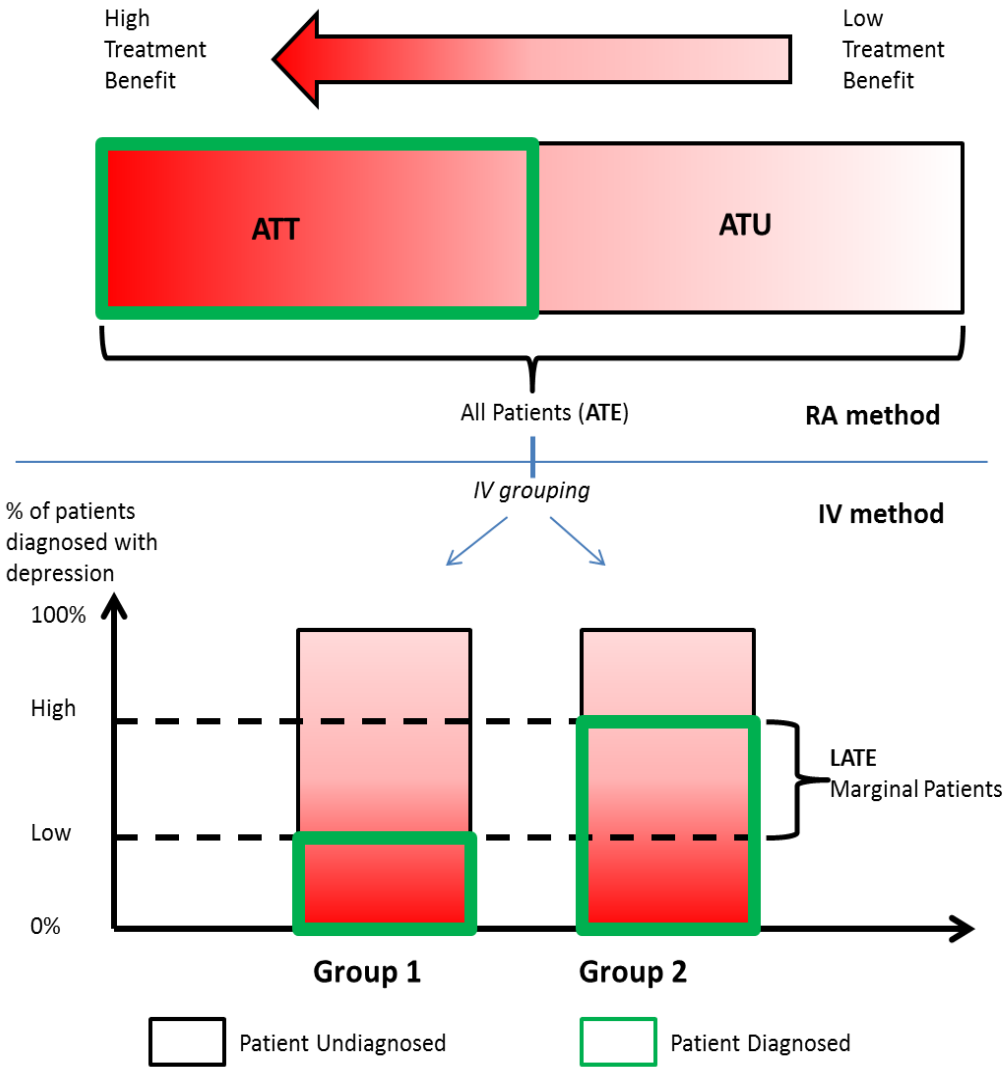
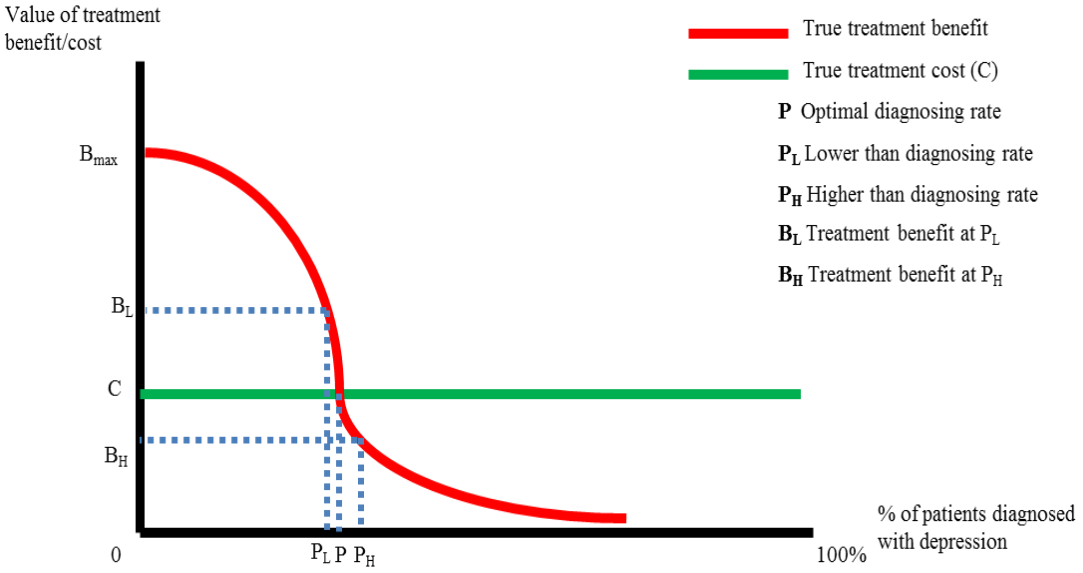
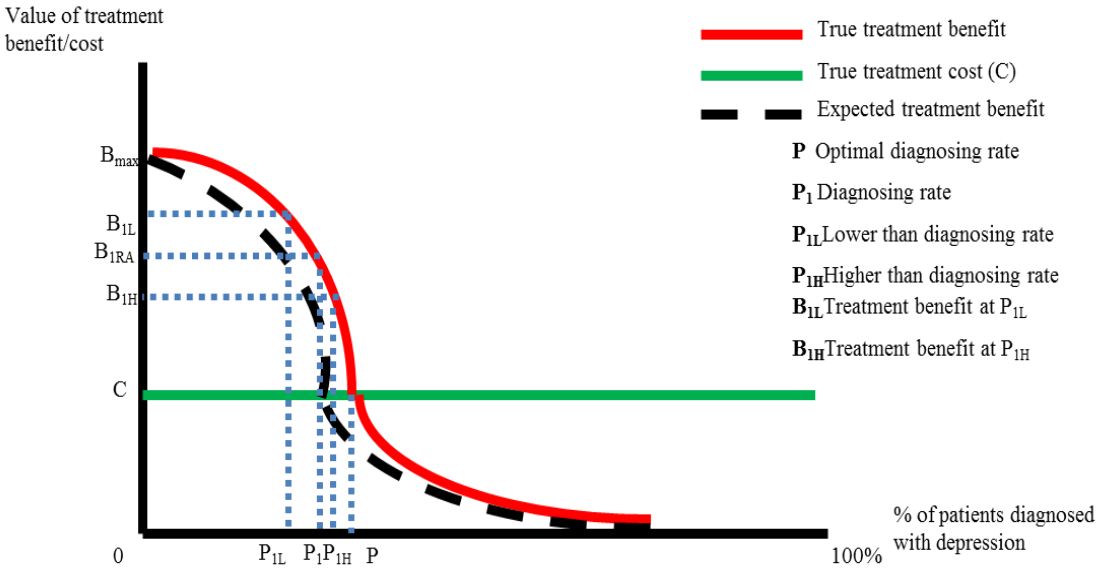


Figure 2.3. Graphical example of interpreting risk adjustment and instrumental variables estimators and depression diagnosis rates



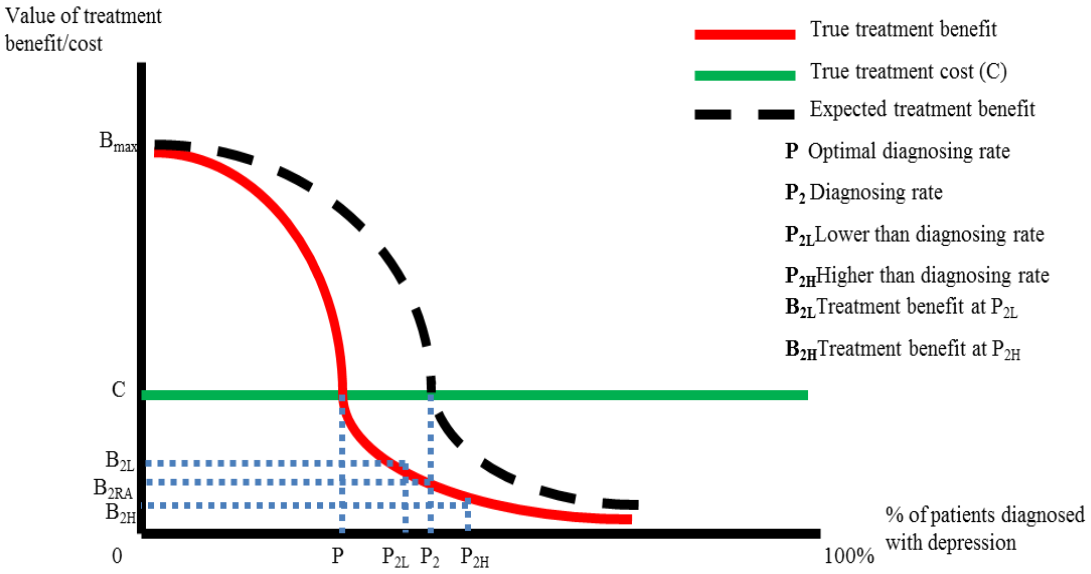
a. Correct estimate

Figure 2.3. Continued



b. Underestimate

Figure 2.3. Continued



c. Overestimate

CHAPTER III

THEORETICAL MODEL

Overview

A *health production function* is often used as a conceptual tool to portray the true relationship among factors affecting individual patient health.[188, 189] These factors may include depression diagnosis. Prior research suggests that the relationship between diagnosing depression and patient health is heterogeneous.[45, 69-73] Research is needed to better understand this heterogeneous relationship across patients. We used a health production function to portray this heterogeneity. In addition, this study exploited variation in depression diagnosing across patients in practice to evaluate the health production function between depression diagnosing and patient health. In practice, physicians make depression diagnosing decisions after interacting with patients. As a result, the diagnosing variation we propose to use in this study was based on variation in physician diagnosing decisions. The properties of estimates from our estimators relative to understanding the health production function depend on assumptions related to the depression diagnosing decision. Therefore, it is necessary to construct a theoretical model of physician decision to diagnose depression through which to interpret our resulting estimates. This section described health production function and physician depression diagnosing choices to show how the effects of physician depression diagnosing decision on outcomes can be analyzed to make inferences on the relationship between depression diagnosing and patient health outcomes.

Integrating treatment-effect heterogeneity into a health production function

Treatment-effect heterogeneity is first discussed here and will be adapted later to diagnosing-effect heterogeneity. The health production function has been used as the theoretical framework to illustrate the relationship between health outcomes and a set of "inputs", including demographic characteristics, healthcare service use, and clinical

factors.[188, 189] In a health production function specification that incorporates treatment-effect heterogeneity, Brooks et al. interacted treatment with factors affecting treatment effectiveness, producing a health production function with treatment effects varying across patients with the interacting factors.[87, 88, 190] The health production function with treatment-effect heterogeneity is useful to delineate factors affecting outcomes and describe how factors that are related to treatment decisions affect outcomes.

(1) $Y = g(T(X_1,X_2), X_2, X_3)$

Y: Outcome given a certain medical condition.

T: Treatment indicator; T = 1 if the patient receives the treatment, T = 0 if the patient does not receive the treatment.

X_1: Factors that affect treatment effectiveness but do not directly affect the probability of being cured.

X_2: Factors that affect treatment effectiveness and also directly affect the probability of being cured.

X_3: Factors that directly affect the probability of being cured but do not directly affect treatment effectiveness.

An example of X_1s could be genetic factors that make treatment more effective in some patients than others, but have no direct effects on outcomes. Genetic polymorphism is suggested to impact how patients respond to granulocyte colony-stimulating factor, a cancer treatment that makes granulocyte colony-stimulating factor more active in some patients than others, but it does not affect outcome directly.[191] An example of X_2s could be patient underlying disease severity that affects treatment effectiveness and directly affects the probability of being cured. Fever as a disease severity measure of otitis media is suggested to directly impact how otitis media patients respond to antibiotic use and health outcomes.[192] An example of X_3s could be patient socioeconomic characteristics. Specifically, patients who have higher incomes and education levels may have better health than those with lower income and education levels.[193]These factors directly affect

the probability of being cured, but do not affect treatment effectiveness. This health production function model above focuses on treatments, but our model focused on diagnosing.

Integrating diagnosing-effect heterogeneity into a health production function

This dissertation adapts the treatment-focused health production function described above and the concept of treatment-effect heterogeneity to assess the effects of diagnosing depression for patients with acute myocardial infarction (AMI). Based on existing evidence, we theorize that the effects of diagnosing depression post-AMI vary with factors such as depression severity [45, 69-73], physical function,[60, 76, 80] overall health,[6, 53, 79] and contextual factors[146-148]. Compared with the treatment-focused health production function (Equation (1)), we cannot think of any factors of X_1 in our model. Therefore, our model includes X_2 (depression severity, physical function, overall health, and contextual factors) and X_3 (other factors that affect patient outcomes).

(2) $H_{hi} = f(D(S_i(F_i, O_i, C_i)), S_i, F_i, O_i, C_i, X_i)$

H_i: Health outcome h (e.g. survival, healthcare costs and utilization) for patient i.

D_i: Depression diagnosis for patient i (1 = diagnosed with depression, 0 = not diagnosed with depression). $D(S_i)$ describes that the effect of depression diagnosis on health is heterogeneous across patients based on depression severity (S) that can be modified by physical function (F), overall health (O), and contextual factors (C);incorporating heterogeneous effects of diagnosis allows treatment effects to vary across patients with different values of characteristics of S, F, O, and C.

S_i: depression severity for patient i. Depression severity is theorized to affect the effectiveness of diagnosing depression and also directly affect the health outcome. The more severe depression the patient has, the less likely the patient has better health outcome regardless of depression diagnosis. Depression severity (S) can be modified by patient "i's" physical function (F)[60, 76, 80], overall health (O),[6, 53, 79] and contextual factors

(C)[146-148] that affect the effectiveness of depression diagnosis through depression severity ($S = S(F, O, C)$).

F_i: physical function for patient i. Physical function is theorized to affect the effectiveness of diagnosing depression through depression severity and also directly affect the health outcome. The worse physical function the patient has, the less likely the patient has better health outcome regardless of depression diagnosis.

O_i: overall health for patient i. Patient overall health is theorized to affect the effectiveness of diagnosing depression through depression severity and also directly affect the health outcome. The worse overall health the patient has, the less likely the patient has better health outcome regardless of depression diagnosis.

C_i: contextual factors (e.g. neighborhood problems, walkability, socioeconomic disadvantage, residential mobility, urban living, and climate)[146-148] that are theorized to affect the effectiveness of diagnosing depression through depression severity and affect patient outcomes.

X_i: Other factors directly affecting the outcome for patient i (e.g. demographic characteristics, healthcare service use, and comorbidities) that do not affect diagnosing effectiveness.[27, 28, 36, 106, 194, 195]

Model of the physician decision to diagnose depression

In general, depression diagnosis involves patient decision to seek professional care for depression and physician decision to diagnose depression. The decision to seek professional care may vary with ability and desire to see a physician. However, this dissertation focuses on a sample of patients hospitalized with AMI who are already in the healthcare system and would need to have follow-up visits for ongoing treatment. The decision to seek care in this sample is less critical. Therefore, we only discussed the model of physician decision to diagnose depression. To investigate the relationship between individual patient outcome and depression diagnosing, we need to exploit variation in depression diagnosing decisions in practice. Given the evidence of depression

treatment-effect heterogeneity, the model needs to incorporate the possibility of *essential heterogeneity*, where treatment effectiveness varies across patients and physician decision making reflects the expected treatment effects.[69, 70] The inferences that can be made from variation in these decisions require a conceptual model explaining why these decisions are made. The model also needs to provide instrument candidates for IV analysis to answer the "right rate" question. In addition, the model needs to be comprehensive, with the ability to describe potential confounders that affect both diagnosing decisions and patient health outcomes that are particularly important for observation studies. A comprehensive model with the ability to identify factors affecting diagnosing decisions and patient health outcomes also allows researchers to describe the assumptions and provide context to validate assumptions underlying each estimator in analysis.

Several theories have been used to describe clinical decision making including diagnosis and intervention. Two theories discussed in this section represent "ideal end-points on a continuum of clinical decision making" between pure intuition and analytical thinking, while another theory is a mixture of both on the continuum.[196, 197] The theory of intuitive decision making suggests that physicians respond intuitively and use available information to make clinical judgements.[196, 197] Under the theory of intuitive decision making, a clinical decision is generated effortlessly and below the level of consciousness. In contrast, the theory of analytical decision making suggests that physicians respond slowly and use additional information they have collected actively.[196, 197] Under the theory of analytical decision making, the clinical decision is a rational and deliberate judgment with application of conscious rules and criteria acquired through learning. The dual-process theory integrates both intuitive and analytical thinking in the clinical decision making process.[196, 197] This theory theorizes that physicians mostly first formulate diagnostic hypotheses and management options intuitively and rapidly and then test the diagnostic hypotheses analytically to make a clinical decision. These three theories have helped researchers to better understand generally how physicians make

clinical decisions.[196, 197] However, they are not helpful in conceptualizing the specific factors that affect clinical decision making, because factors affecting clinical decisions are not specified in the three theories. A conceptualization of these factors is critically needed when evaluating the properties of treatment-effect estimates using observational data.

Another decision theory to describe diagnosis and treatment problems was introduced by Ginsberg and Offensend.[198] They modeled diagnosis-treatment decisions with a decision tree that maximizes physician satisfaction over all possible lab tests, diagnosis, and treatment decision making and patient health outcomes. The authors acknowledged that this theory is complicated and hard to be applied across various diagnosis and treatment problems. This theory does not provide a conceptualization of what physicians actually do, specify factors affecting clinical decision making, incorporate the concept of essential heterogeneity, or serve as a basis for instrument searching. Thus, a conceptual model is needed that specifically describes factors that affect actual physician clinical decision making.

In the economics literature, utility-based models have been used to describe physician behavior. Utility can be seen as a measure of a person's overall well-being, happiness, and satisfaction and is used as a way to describe decision-maker preferences.[199] Utility was originally described in economics as gains by an individual from consuming goods and services directly.[199] Lancaster and Becker argued that utility functions based on goods and services lack a "story" linking to underlying "characteristics".[200, 201] To Lancaster and Becker, "characteristics" are fundamental aspects of life or goals that can be affected by the consumption of goods or services. In Lancaster and Becker's utility theories, utility is derived from the underlying characteristics that are "possessed" by goods and services. Additionally, conceptual relationships between utility and goods and services can be very complex, especially

when consuming a good or service can affect more than one underlying characteristic.[200, 201]

The Lancaster and Becker utility approach can be characterized by their distinct concepts: *preferences, beliefs, and constraints*.[200] Changes in "characteristics" directly affect utility. For example, if having a highly regarded reputation is a characteristic for physicians and using the newest treatment "possesses" the reputational characteristic, then using the newest treatment may lead to higher reputation for physicians and the higher reputation may increase their utility. The relationships between "characteristics" and utility vary across decision makers based on decision makers' *preferences* across characteristics. For example, if higher income is a characteristic for physicians, some physicians may value additional income more than others. In this case, an increase in income may lead to more increased utility for the former physicians. Choices may affect "characteristics," and *beliefs* describe how decision makers believe choices will affect "characteristics" a priori. This idea is also known as a household production function in which decision makers really value what is produced from goods and services, instead of goods or services themselves. For example, if having a highly regarded reputation is a characteristic for physicians and physicians believe the newest treatment affects reputation, physicians with stronger beliefs in the newest treatment benefit may be more likely to prescribe the treatment than those without strong beliefs. Decision-maker choices are often limited by *constraints,* such as available time and resources. For example, if physicians do not have certain equipment, their choices are limited to tests or assessments that do not use that equipment.

Using the Lancaster and Becker approach, McGuire and Pauly applied utility modeling with *preferences, beliefs, and constraints* to describe provider behavior.[202] In McGuire and Pauly's model, physician utility is assumed to be positively affected by the characteristics of physician practice net revenue, leisure time, and reputation. Net revenue is profit that equals revenue minus cost. The physician utility increases with reputation

and reputation is believed to diminish with bad behavior. Physicians prefer higher profit, leisure time, and reputation. However, physicians believe that more new treatments lead to higher profit, less leisure time and a non-linear relationship with reputation in which more visits lead to higher reputation at first, and then additional visits are associated with lower reputation.

Our model of the physician decision to diagnose depression is based on *preference, beliefs, and constraints* utility-based theoretical model. We theorize that a physician chooses to diagnose a patient so to maximize the following physician utility (U) function.

(3) $U_j = U(\pi, H, L, R; \delta_j)$

In equation (3), the utility of physician "j" (U_j) is assumed to be affected by the attainment of four different characteristics: physician profit (π), expected patient health (H), physician leisure time (L), and physician reputation (R). δ_j is a parameter vector summarizing physician "j's" ***preferences*** relating changes of physician utility with weighted changes among the characteristics. Preference weights across characteristics can vary across physicians, but general assumptions about "marginal utility" are assumed to apply across physicians. Marginal utility is defined as changes in utility resulting from changes in each characteristic. It is assumed that an increase in each of the four characteristics is associated with increased physician utility (U). Marginal utility can be written as the first derivative of utility for each characteristic is positive, $U_\pi > 0$, $U_H > 0$, $U_L > 0$, and $U_R > 0$. Furthermore, the marginal utility of each characteristic is assumed to decrease as a higher level of each characteristic is reached. It can be denoted by a negative relationship for the second derivative of physician utility for each characteristic, $U_{\pi\pi} < 0$, $U_{HH} < 0$, $U_{LL} < 0$, and $U_{RR} < 0$. That is, physician utility increases are smaller with increases in physician profit (π), expected patient health (H), physician leisure time (L), and physician reputation (R) at higher baseline levels of each characteristic. For example,

an increase in physician reputation will increase utility more to a physician who has a lower initial reputation level than a physician who starts at a higher reputation level.

In application of the household production function from Lancaster and Becker to the physician decision to diagnose a patient, physician diagnosing decisions are theorized to affect physician utility through how physician "j" diagnoses patient "i" in the local area "t" and how physicians believe their decisions will affect each characteristic.

(4) $H_{ijt} = H_0 (S_i, F_i, O_i, C_i, X_i) + \lambda_{ijt} (S_i, P_t, Y_i) * D_{ijt}$

(5) $\pi_{jt} = \varphi_{jt} * (D_{ijt} + B_{jt}) + \tau_{jt} * (N (M_t) - (D_{ijt} + B_{jt}))$

(6) $L_{jt} = T_j - (\psi_{jt} * (D_{ijt} + B_{jt}) + \omega_{jt} * (N (M_t) - (D_{ijt} + B_{jt}))$

(7) $R_{jt} = R (\rho_{jt}(D_{ijt} + B_{jt}), P_t)$

The four equations describe physician beliefs as to the relationship between depression diagnosing and the four characteristics affecting physician utility. It is important to note the distinction between equation (4) which shows physician "j's" beliefs about the diagnosing effects on patient outcomes for patient "i" in area "t", and equation (2) which represents the true effects of diagnosing depression on patient outcomes. H_{ijt} is expected patient "i's" health outcome from physician "j's" perspective in area "t" that is modeled as patient baseline health plus an expected diagnosing effect. Patient baseline health (H_0) is a function of patient underlying depression severity (S_i), physical functional status (F_i), overall health (O_i), contextual factors (C_i), and other factors (X_i), such as patient demographic characteristics, healthcare service use, and comorbidities.[27, 28, 36, 106, 194, 195] In addition, S_i, F_i, O_i, C_i, and X_i in equation (4) are equivalent to those in equation (2). D is depression diagnosing decision that equals 1 if a patient receives a depression diagnosis, 0 otherwise. The parameter λ represents physician beliefs about the effects of diagnosing depression on patient "i's" health outcome, while equation (2) describes the true relationship between diagnosing depression and health outcome for patient "i". The parameter λ is theorized to be a function of patient depression severity (S_i) (modified by physical function, overall health,

and contextual factors), average beliefs about the effects of depression diagnosing on health outcome across physicians in the local area "t"(P_t), and other factors (Y_i) such as patient's ability to articulate depressive symptoms with physicians and willingness to accept a depression diagnosis, physician's ability to diagnose depression and willingness to accept depression, and systematic approach to detecting and managing depression in the local healthcare system.[46, 151] These other factors (Y_i) have been discussed in detail in the literature review section. It is expected that the more severe depression a patient has and the higher the average local area benefit beliefs, the stronger the physician believes that a diagnosis of depression will help the patient.

In equation (5), π is physician "j's" weekly profit in area "t", which is theorized to be generated from providing healthcare services to patients without depression diagnoses and care for diagnosed depression patients. The parameter φ_{jt} represents physician "j's" beliefs about his/her profit after diagnosing a patient with depression in area t; ($D_{ijt} + B_{jt}$) is the number of patients who were diagnosed with depression by physician "j" in a week if the patient "i" receives a depression diagnosis. An additional patient who is diagnosed with depression in the local area would lead to additional physician profit through office visits, diagnostic assessments, and depression treatments provided. The parameter τ_{jt} is physician "j's" beliefs about his/her profit from a patient without a depression diagnosis in area "t"; N is the total number of patients physician "j" has seen in a week that is a function of local physician supply (M_t); (N (M_t) - ($D_{ijt} + B_{jt}$)) is the number of patients without depression diagnoses for physician "j" in a week if the patient "i" does not receive a depression diagnosis. For patients hospitalized with AMI, the primary treating physicians would be more likely to be cardiologists. The cardiologists may believe additional profit after diagnosing an AMI patient with depression may be lower than additional profit from an AMI patient without depression diagnosis. In this case, cardiologists may focus more on patient's cardiovascular problems with beliefs in higher

additional profit instead of spending more time on depression assessment and treatment plans with beliefs in lower additional profit ($\varphi_{jt}<\tau_{jt}$).

In equation (6), L is physician "j's" leisure time in area "t" in a week, which is theorized to be the total time (T_j, e.g. 40 hours) available to a physician minus the time the physician spends on his/her patients. The parameter ψ_{jt} represents physician "j's" beliefs about time spent on additional patient diagnosed with depression in area "t"; ($D_{ijt} + B_{jt}$) is the number of patients who were diagnosed with depression by physician "j" in a week if the patient "i" receives a depression diagnosis. ω_{jt} is physician "j's" beliefs about time spent on additional patient without a depression diagnosis in area "t"; ($N(M_t) - (D_{ijt} + B_{jt})$)is the number of patients without depression diagnoses for physician "j" in a week if the patient "i" does not receive a depression diagnosis. If physician "j" believes more time spent on a patient diagnosed with depression than on a patient without a depression diagnosis ($\psi > \omega$), an additional depression diagnosis ($D_{ijt} = 1$) would lead todecreased leisure time for physician "j". From equations (5) and (6), if $\psi > \omega$, the additional profit per physician minute from treating an additional patient diagnosed with depression is less than treating a patient without depression. In other words, an additional depression diagnosis would lead to increased time spent on less profitable services. Cardiologists may have many patients in a week and often have multiple tasks during an office visit, including examining and managing known cardiovascular disease, overall health maintenance, and paperwork.[46] As a result, they may be reluctant to assess depression, which requires time to reach closure and develop a management plan.[46]With a large number of patients and limited time in a week, additional depression diagnoses would result in less physician leisure time and lower physician profit.

In equation (7), physician "j's" reputation (R_{jt}) is theorized to be a function of $\rho_{jt,}$ the share of patients diagnosed with depression by the physician ((D + B)/N) in area "t", and average beliefs of the effects of diagnosing depression on health outcomes for physicians in the area "t" (P_t).It is assumed that physician diagnosing rates substantially

lower or higher than area norms (reflected by the local average beliefs) will put a physician's reputation at risk. In this case, physician reputation increases with an additional depression diagnosis ($D_{ijt} = 1$) if the share of patients diagnosed with depression by the physician is below the local area diagnosis rate, but decreases if the share of patients diagnosed with depression by the physician is above the local area diagnosis rate.

In this model, a physician will diagnose depression if his/her expected utility from an additional depression diagnosis is greater than his/her utility without a depression diagnosis. By substituting equation (4)-(7) into equation (3), the expected net utility for a physician can be written as physician utility from diagnosing depression minus the utility from not diagnosing depression. For clarity, the subscripts are dropped in the following equations.

(8) $NU = U(H_0(S, F, O, C, X) + \lambda(S, P, Y)), \varphi * (B + 1) + \tau * (N(M) - (B + 1)), T - (\psi * (B + 1) + \omega * (N(M) - (B + 1))), R((B + 1)/N, P); \delta) - U(H_0(S, F, O, C, X), \varphi * B + \tau * (N(M) - B), T - (\psi * B + \omega * (N(M) - B)), R(B/N, P); \delta)$

An additional depression diagnosis increases physician utility through physician beliefs in expected increases in patient health (via λ), physician profit (via φ) if profit per patient diagnosed with depression is believed higher than profit per patient without a depression diagnosis by the physician ($\varphi > \tau$), and expected increases in physician reputation (R) if the physician's share of diagnosing depression is below area norms. On the other hand, an additional depression diagnosis decreases physician utility through expected decreases in physician reputation (R) if the physician's share of diagnosing depression is above area norms. Diagnosing depression also decreases physician utility through expected decreases in leisure time (via ψ) if patients diagnosed with depression require more physician time than those without depression diagnosis and through expected decreases in physician profit(via τ) if profit per patient diagnosed with depression is less than profit per patient without a depression diagnosis ($\varphi < \tau$).

Furthermore, physician net utility associated with each characteristic varies with physician preferences (δ) over the characteristics and the initial level of each characteristic prior to each diagnosing decision. Suppose that patients diagnosed with depression require more physician time but yield less profit gains than those without depression diagnoses. For instance, if a physician with abundant leisure time may value leisure timeless than other characteristics, the physician may be more likely to spend time assessing depressive symptoms and make a depression diagnosing decision with high beliefs in the effects of diagnosing depression on health outcomes than those with less leisure time.

Given equation (8), the probability of giving a depression diagnosis can be rewritten as follows

(9) $P(D = 1) = P(NU > 0) = P(NU(S, F, O, C, X, P, Y, M, \lambda, \varphi, \tau, \psi, \omega, \delta) > 0)$

The probability of diagnosing depression equals the probability that net utility for a physician is greater than 0. D represents the physician decision to diagnose depression.

The specification in equation (9) has several implications for this research effort. Equation (9) lists the set of concepts theorized to be related to a physician's diagnostic choice. Factors in both equations (2) and (9) are confounders, such as patient underlying depression severity, physical function, overall health, contextual factors, demographic characteristics, healthcare service use, and comorbidities. Factors only in equation (9) but not in equation (2) are potential candidates for instruments in IV analysis, such as physician's beliefs about the effect of depression diagnosis, local average beliefs about the effect of depression diagnosis, and physician supply in the local area. In theory, these potential instruments affect physician decision to diagnose depression through their effects on physician net utility.

Physician beliefs about the effects of diagnosing depression in the local area (P) is theorized to affect physician net utility through expected patient health via beliefs in health benefits associated with each diagnosis and through physician reputation. We

theorize that physicians in an area with strong positive beliefs about the benefits associated with diagnosing depression will also tend to hold strong positive beliefs in the benefits and be more likely to make a depression diagnosing decision. Additionally, areas where physicians share strong positive beliefs in the benefits of diagnosing depression tend to have higher diagnosis rates, and it is less likely that physician reputation will be placed at risk by diagnosing a larger proportion of patients with depression.

Physician supply in the local area (M) is theorized to affect physician net utility through income and leisure time. That is, physicians in areas with a higher supply of physicians and fewer patients per physician will have a lower number of patients, resulting in lower profit and more leisure time at baseline than physicians in areas with a lower supply of physicians and more patients per physician. Thus, the net utility related to an additional diagnosing decision will be higher for physicians in these areas than areas with more patients per physician. Consequently, physicians in areas with a higher supply of physicians and fewer patients per physician (e.g. more cardiologists, general practitioners, and psychiatrists in local areas) may be more likely to make a depression diagnosing decision. Additionally, we theorize that the more psychiatrists in an area who are able to specialize in depression assessment and management, the more likely these psychiatrists will be knowledgeable about the potential benefits of depression diagnosis for their patients. It is theorized that increased physician knowledge will influence diagnosing decisions, but the direction of the effect is a function of physician beliefs in the diagnosing benefits for each patient.

In the methods section, we further discussed what properties a good instrument candidate possesses in detail and the empirical implications that are developed from the utility-based theoretical framework.

CHAPTER IV

METHODS

Overview

This is a retrospective cohort study with an intention-to-treat study design. We used Medicare claims data to identify patients first diagnosed with AMI. This study examined the effects of diagnosing depression after AMI on patient health and economic outcomes. Innovative analytical approaches were applied using alternative estimators that yield distinct interpretations of estimates for different subsets of the population. In addition, we used chart abstraction data from a convenience sample of patients to attempt to validate the underlying assumptions in each analytical approach and ascertain bounds on the estimated effects of diagnosing depression.

Aim 1

Data sources

Our data come from the Medicare Chronic Condition Data Warehouse (CCW) that was launched by the Centers for Medicare and Medicaid Services in response to the Medicare Modernization Act of 2003. The CCW data includes Medicare fee-for-service (FFS) institutional (inpatient, outpatient, skilled nursing facility, hospice, and home health agency) and non-institutional claims (carrier and durable medical equipment claims), enrollment/eligibility files, and assessment data. The CCW beneficiary summary file provides information on beneficiary demographics, residence ZIP codes, Medicare Part A, B, D enrollment, date/cause of death, summary of beneficiary chronic illnesses by year, healthcare cost, and healthcare resource use. As of 2006, Part D prescription drug event (PDE) data is added, including Part D plan, pharmacy, and prescriber characteristics and medication formulary file. CCW clinical condition flags were made for the initial 21 chronic illnesses, including AMI. To ensure a continual state of improvement for research, 6 additional condition indicators were developed for Medicare beneficiaries. The 27 predefined and standardized medical conditions were developed

using CCW claims to facilitate research on chronic conditions in Medicare beneficiaries and ultimately improve the quality of care and reduce healthcare expenditures. In this study, we used 100% of all Medicare FFS beneficiaries with an AMI during 2007-2008. The analysis also used a supporting dataset with driving distance and time between any two ZIP codes in the United States, Medicare Physician Identification and Eligibility Records (MPIER) file (2006, 4th quarter) with physician identifiers and specialty types, a crosswalk between Unique Physician Identification Number (UPIN) and National Physician Identifier (UPI), Federal Bureau of Investigation (FBI) 2007-2008 Uniform Crime Reports (UCR), United States 2000 Census Data with measures of neighborhood characteristics, and the National Oceanic and Atmospheric Administration (NOAA) National Weather Service data in 2007-2008 with measures of climate.

Research design

This study was a retrospective cohort study using a large observational database from Medicare claims. The cohort included all Medicare FFS enrollees with their first AMI without depression diagnosis in the previous year during 2007-2008. We focused on patients without a prior diagnosis of depression using a new user study design that allows us to assess incident rather than prevalent depression diagnoses post AMI. The study cohort was followed up to death or 1 year after the index admission date to retrieve information on survival, healthcare costs and utilization.

Study population

We selected Medicare beneficiaries hospitalized with a newly diagnosed AMI without prior depression diagnosis in 2007-2008. The index AMI was defined as the patient's first AMI during 2007-2008 without AMIs in the prior 1 year. The admission date of the index AMI was the index date. Individuals were included if they (1) were older than 65 years old at their index AMI to ensure at least 1 year of observation window prior to the index date to observe prior AMIs; (2) did not have AMIs within 1 year prior to the index date; (3) were not enrolled in a health maintenance organization

(HMO) during the 1 year prior to the index date; (4) were enrolled in Medicare Part A and B during the 1 year prior to the index date to ensure observing patient pre-index comorbidities and health service use; (5) were enrolled in Medicare Part D during the 6 months prior to the index date to ensure observing patient pre-index medication use; (6) were discharged and after index hospitalization; (7) were not enrolled in an HMO till death or 1 year after the index date to ensure evaluating healthcare costs; (8) were enrolled in Medicare Part A, B, and D till death or 1 year after the index date or till death to ensure adequate evaluation of healthcare cost and utilization outcomes; (9) resided in the continental United States to ensure driving time between ZIP codes with consistent meaning in the definition of small areas used in this dissertation; (10) resided in a ZIP code with driving information in the supporting ZIP code file; (11) were not diagnosed with depression within 1 year prior to the index date; (12) survived 30, 60, or 90 days after the index date for different observation windows of depression diagnosis. The selected AMI cohort was followed for up to 1 year after the index date or till death. The Medicare CCW data from 2006 to 2009 were used for the identified cohort. The 1-year period before index AMI was used to ensure the patient did not have an AMI and depression within 1 year prior to the index date. Patient pre-index medical conditions and procedures were assessed during the 1 year before the index date using Part A and B data. Patient medication use was assessed within 6 months before the index date using Part D data. Healthcare cost and utilization was calculated after the index date using Part A, B, and D data. In addition, patient demographics were assessed using CCW enrollment/eligibility files.

Unit of analysis

The unit of analysis for this study is the individual patient with AMI aged 66 and older during 2007- 2008.

Key independent variables

The key independent variable for the diagnosing choice-outcome relationship model was whether a patient was diagnosed with depression. International Statistical Classification of Diseases (ICD) 9 codes of MDD, dysthymia, and depression not otherwise specified (NOS) were used to measure depression. Depression diagnosis was set to 1 if a patient had a depression diagnosis within 30 days post index date; 0 otherwise.[203-205] Depression diagnosis was identified using Medicare Part A and B data. Table 4.1 shows depression diagnosis and its coding scheme.

With an intention-to-treat study design, the primary goal was to capture the initial diagnosing decision made for each patient after the index AMI admission date. As in some earlier studies exploring the relationship between depression and outcomes post AMI, we also measured depression diagnosis within 60 days and 90 days after the index date and to evaluate whether the effects of diagnosing depression on outcomes change (only include patients surviving the first 60 days and 90 days after the index date to ensure observing depression diagnosing for each subsample).[203-205] However, depression severity was not well measured in Medicare claims data, because previous studies showed the validity of depression severity measure based on ICD codes is highly debatable.[206, 207]

Dependent variables

The outcome variables for this dissertation were survival, healthcare costs and utilization within 1 year post the index date (Table 4.2). The indicator of 1-year survival equaled 1 if the patient was alive within 1 year post the index date; 0 otherwise. Date of death was obtained from the CCW beneficiary summary file.

Total healthcare cost was a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post index date or till death. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that

allows direct and accurate comparison of healthcare resource use.[208] Total healthcare costs were also analyzed separately into standardized Medicare Part A, B, and D costs in 1 year. Part A cost included all claims from inpatient, skilled nursing facility, home health agency, and hospice; Part B cost included all claims from outpatient, carrier, and durable medical equipment; Part D cost included all claims from prescription drug events. Given both institutional and non-institutional claims within Medicare Part B, we further assessed Part B costs into outpatient (institutional claims), physician fee schedule (non-institutional mainly carrier claims), and others (non-institutional durable medical equipment claims and carrier claims not from physicians).

Corresponding with each part of cost measures, we assessed patient healthcare utilization within 1 year post the index AMI admission. We calculated hospitalization by summing up all inpatient claims with unique claim from and through dates over the 1-year period post the index date or till death. Over the same timeframe, we calculated emergency department (ED) visits using inpatient and outpatient claims, outpatient visits using outpatient claims, physician visits using outpatient and carrier claims, and prescriptions drug use using prescription claims.

Instruments

IV estimators provide estimates of the local average treatment effect for patients whose treatment choice varies by "instruments".[92] A valid "instrument" is a measured factor that has two properties: strongly related to treatment decision, but unrelated to unmeasured confounders or outcomes directly.[93] Based on the model of physician decision to diagnose depression in the theory section, local average beliefs and individual physician beliefs in the effects of diagnosing depression on outcomes are potential instruments. Physicians in local areas with stronger beliefs about the effects of depression diagnosing on health outcomes may be more likely to make a depression diagnosing decision than those in local areas with less strong beliefs. Similarly, individual physicians who hold stronger positive beliefs in the benefits of depression diagnosis on patient

health outcomes may be more likely to diagnose depression than those with less stronger beliefs. The two potential instruments are theorized to directly affect depression diagnosing decision, but do not affect health outcomes unless through their effects on depression diagnosis. In the IV models, only variation in depression diagnosis based on the instruments selected were used to estimate the effects of depression diagnosing on health outcomes. Therefore, we used measures of local area depression diagnosing styles and individual physician practice styles of depression diagnosis in two IV models as the basis to develop instruments.

In this study, measures of local area depression diagnosing styles were developed using depression diagnosing patterns post AMI for patients living in local areas based upon driving time. The first step of creating instruments was to define local areas around each ZIP code. Local areas were created using the driving area for clinical care (DACC) to capture physician practice styles across local areas.[96] The DACC method characterizes the average treatment choices for patients within driving-time areas around each ZIP code to reflect local area physician practice styles, but does not predefine an area where ZIP codes are assigned. We applied the DACC method to capture local depression diagnosing styles for AMI patients living within driving-time areas around each ZIP code. CCW enrollment and eligibility files were used to ascertain patient ZIP codes. A DACC-defined area was expanded around each ZIP code until a minimum number of AMI patients were found. The threshold number of AMI patients around each ZIP code varied from 50 to 200 persons by 10 to examine whether IV estimates changed with local area sizes.

The next step was to estimate a local area diagnosing ratio (ADR) for each ZIP code-defined area. We first calculated the average number of patients receiving a depression diagnosis in the local area defined by DACC on ZIP code level. Then, we estimated the depression diagnosis choice model by regressing the binary variable for depression diagnosing on measured factors that affect depression diagnosing decision.

Thus, the probability that each patient received a depression diagnosis given individual characteristics was calculated in the model. The ADR for ZIP code "z" was estimated as the proportion of patients receiving a depression diagnosis around each ZIP code divided by the average predicted probability of the same patients to receive the diagnosis in that ZIP code (see the equation below). The variation in depression diagnosis identified from this approach was unrelated to the measured factors that affected depression diagnosing decision. An ADR greater than 1 indicates that a local area practice style diagnoses more depression than expected given patient characteristics in the local area. An ADR less than 1 indicates a local area practice style that diagnoses less depression than expected.

$$\text{Area Diagnosing Ratio } z = \frac{\left(\sum_{i=1}^{n} \text{Diz}\right)/nz}{\left(\sum_{i=1}^{n} \widehat{\text{Diz}}\right)/nz}$$

i = 1, 2, 3, …,nz (the number of patients residing in the ZIP code"z")

z = ZIP code "z"

D_{iz} =1 if patient "i" in the area associated with ZIP code "z" receives a depression diagnosis, 0 otherwise

$\widehat{Diz}$ = predicted probability of patient "i" in the area associated with ZIP code "z" to receive a depression diagnosis

In the IV model, instruments were specified using binary variables based on the distributions of ZIP code-based ADRs across patients. For instance, suppose 0.8, 0.9, 1, and 1.1 represent the 20^{th}, 40^{th}, 60^{th}, and 80^{th} percentiles of the ADR distribution. Binary variables were created to categorize areas into five groups (ADR<0.8, 0.8<ADR<0.9, 0.9<ADR<1, 1<ADR<1.1, ADR>1.1). To assess the robustness of the IV estimates to ZIP code classifications, we estimated IV models based on different percentile cutoffs of the ADR (tertiles, quintiles, and deciles).

Furthermore, 3 sets of sensitivity analyses were performed. First, patients with prior bipolar disorder, psychotherapy and antidepressant use who were not documented with a depression diagnosis in Medicare claims data might have depression prior to the

index AMI admission. Therefore, to obtain a cleaner sample of AMI patients without prior depression diagnosis, we further excluded patients with prior bipolar disorders, psychotherapy and antidepressant use measured in Medicare claims data, to examine whether the estimates of the effects of depression diagnosis on patient outcomes were consistent between our main study sample and the cleaner sample. Second, since each patient's ADR was calculated using patients living in that local area included that patient, it is possible that the patient ADR was correlated with that patient's unmeasured characteristics. Therefore, we test the robustness of our ADR-based instrument by excluding the patient from the ADR calculation for that person's ZIP code level ADR. Third, we assessed whether the IV estimates were consistent by using unadjusted depression diagnosis rates in local areas (excluded the patient from the unadjusted area depression diagnosis rate calculation).

In addition, alternative instruments of individual physician practice styles of depression diagnosis were measured. We used CCW claims with physician identification numbers (UPIN or NPI) and a crosswalk between UPIN and NPI to track each individual physician. With patient AMI admission date as the index date, we used a 6-month period before the index date as the measurement period for individual physician's preferences of depression diagnosis.[209] First, every physician that each patient made contact with within 30/60/90 days post AMI admission was selected. Second, a broader sample was created if Medicare patients (1) did not have AMI in the prior year; (2) did not enroll HMO in the prior year; (3) had Medicare Part A and B in the prior year to ensure observing any prior 1-year AMI admission; (4) did not enroll in HMO within 30/60/90 days after the index AMI admission; (5) had Medicare Part A and B within 30/60/90 days after the index AMI admission; (6) were alive within 30/60/90 days after the index AMI admission to ensure observing depression diagnosis after AMI admission. Third, the total number of previous patients from the broader sample seen by the physician in the first step and the number of these patients with a depression diagnosis were calculated during the 6-month

period before AMI admission date in the original sample. Forth, for all the physicians a patient saw within 30/60/90 days post AMI admission, the total number of previous patients and the number of those with a depression diagnosis were summed up for that patient. Lastly, the "average" individual physician practice styles of diagnosing depression were calculated as the proportion of previous patients seen by the physicians (that patient saw within 30/60/90 days post AMI admission) with a depression diagnosis.

Control variables

Table 4.3 shows a list of variables in the theoretical models of depression diagnosing choice and its outcomes and their potential measures in this study. Control variables in the model include patient demographic characteristics, pre-index medical conditions, pre-index procedures, pre-index medication use, and contextual factors. Depression severity is not accurately measured using ICD 9 codes.[206, 207] Physical function and overall health are unmeasured using claims data.

Empirical implications

In the theoretical model, equation (2) illustrates factors affecting patient health outcome and equation (9) illustrates factors affecting diagnostic decision making. To operationalize the theoretical framework, an empirical model was used to serve as the basis of making inferences on the diagnosing-outcome relationship from alternative estimators. Estimates from RA and IV estimators yield distinct interpretations of the effects of diagnosing depression on health outcomes. RA estimators yield average effects of diagnosing depression on patients diagnosed with depression. IV estimators yield local average effects of diagnosing depression for patients whose depression diagnosing decision is affected by the instruments.

For clarity, we used linear models in this section to discuss the estimation model and to interpret parameter estimates. Since depression severity (S), physical functioning (F), and overall health (O) were unmeasured or not well measured in claims data, the following two equations represent the empirical model based on the theoretical model

discussed earlier. Equation (10) shows the estimating equation of the relationship between patient outcome (H) and factors affecting health outcome. Parameter β_1 is the effect of depression diagnosing (D) on health outcome. E represents measured confounders that affect health outcomes and depression diagnosis, including contextual factors (C) and demographic characteristics, comorbidities, and healthcare service use (X). u is an error term of all unmeasured factors that affect health outcome, such as patient underlying depression severity, physical function, and overall health. Equation (11) shows the estimating equation of the relationship between depression diagnosing and factors affecting diagnostic decision making. Instruments (I) need to satisfy two requirements: strongly related to depression diagnosing decision, but unrelated to health outcome unless through depression diagnosis. According to our theoretical model, potential instruments are local average physician beliefs and individual physician beliefs about the effects of depression diagnosing on health outcomes. v is an error term of all unmeasured factors that affect diagnosing choice, such as depression severity, physical function, overall health, and other factors from patients, physicians, and the local healthcare system discussed in the theory and literature review sections.

(10) $H = \beta_0 + \beta_1 * D + \beta_2 * E + u$

(11) $D_i = \theta_0 + \theta_1 * E + \theta_2 * I + v$

To interpret estimates of the effects of depression diagnosing on health outcome (β_1), linear models of health production function and physician decision to diagnose depression are needed with unmeasured confounders. Equation (12) describes the relationship between diagnosing depression and patient outcome. A represents unmeasured confounders that affect outcomes and diagnosing decision, including depression severity, physical function, and overall health. Therefore, A is the X_2 variable in equation (1). Furthermore, the effects of depression diagnosing on health outcome vary across patients with different depression severity, physical function, and overall health.

Equation (13) describes the theoretical model of diagnosing decision. For clarity and simplicity, we use linear models to discuss the theoretical model.

(12) $H = \iota_0 + \iota_1 * A + (\iota_{20} + \iota_{21} * A) * D + \iota_3 * E$

(13) $D = \kappa_0 + \kappa_1 * A + \kappa_2 * E + \kappa_3 * I$

RA and IV estimators yield average effect estimates for different subsets of the population.[87, 88] In this study, RA estimators yield the average effects of diagnosing depression for patients who received a depression diagnosis.[87, 88]

(14) $E_{RA}(\beta_1) = \iota_{20} + \iota_{21} * E(A|D=1) + \kappa_{1*}\iota_1$

The expected value of β_1 reflects the average effect of diagnosing depression for patients who received a depression diagnosis ($\iota_{20} + \iota_{21} * E(A|D=1)$), plus confounding bias from unmeasured confounders ($\kappa_{1*}\iota_1$). Proof of the expectation of parameter estimates can be found in the cited economic literature.[81, 170, 190, 210] E (A|D=1) equals the average unmeasured confounders (e.g. depression severity, physical function, and overall health) for patients who were diagnosed with depression. Parameter ι_1 reflects the relationship between patient health outcome and unmeasured confounders and parameter κ_1 reflects the relationship between depression diagnosing decision and unmeasured confounders. Parameter $\beta_1$is an unbiased estimate of the average diagnosing depression effect for the diagnosed patients if the assumptions that patient unmeasured confounders (e.g. depression severity, physical function, and overall health) have no direct effect on survival outcome ($\iota_1 = 0$) or have no effect on whether or not a patient received a depression diagnosis ($\kappa_1 = 0$) are true. Given that the theoretical framework indicates that depression severity, physical function, and overall health directly affect both health outcome and diagnostic decision making, β_1 is a biased estimate of the average effect of diagnosing depression on health outcome for the diagnosed patients. If patients who are diagnosed with depression are more likely to have severe depression, worse physical function, and worse overall health, the effects of depression diagnosis on health outcome (β_1) would be biased low. If patients who are diagnosed with depression are less likely to

have severe depression, worse physical function, and worse overall health, the effects of depression diagnosis on health outcome (β_1) would be biased high.

In contrast, IV estimators yield local average effects of diagnosing depression for the subset of patients whose depression diagnosis is affected by the instrument.[87, 88] An IV estimator yields a consistent estimate of the effect of diagnosing depression on patient health outcome for the marginal patients if the instrument selected satisfies two requirements: strongly related to depression diagnosis, but unrelated to health outcome and unmeasured confounders.[93] Two IV models with two different instruments were employed in this dissertation to assess the effects of diagnosing depression for patients whose diagnosing decision was affected by the instrument selected. One instrument used in this study was based on the concept of local area depression diagnosing styles. In the theoretical model, we assume that average beliefs about the effect of depression diagnosing for all physicians in the local area (P) affect diagnosing depression directly, but only have indirect effect on patient health outcome through the effect of diagnosing depression. As a result of the assumptions, measures of the average beliefs about depression diagnosing effect for all physicians in the local area (P) are good candidates of valid instruments for IV analysis. For the other IV model, the instrument is based on individual physician practice styles of depression diagnosis that is assumed to directly affect diagnosing decision, but does not affect health outcome unless through its effects on depression diagnosis.

In previous IV research, a nonparametric two-stage least squares (2SLS) estimator has been used to estimate treatment effects.[87, 88, 94, 95, 97, 113-115, 211] The 2SLS estimator yields consistent estimates without regard to the distributions of error terms.[212] In the2SLS estimation model, the first stage estimates the diagnosing choice equation and tests whether the instruments selected describe a significant portion of variation in diagnosing choice. The predicted probability of getting a depression diagnosis was calculated from the first stage equation (11). In the second stage, we estimated equation

(10) by replacing the actual decision of diagnosing depression with the predicted probability of getting a depression diagnosis from the first stage equation (13). After controlling for the measured factors in the two stages (C: contextual factors; X: patient demographics, healthcare service use, and comorbidities), only variations in diagnosing choice stemming from the instruments were used to estimate the effect of diagnosing depression on patient health outcome. Since local area depression diagnosing styles were theorized to be unrelated to health outcome and unmeasured confounders, the IV method provides natural experiments on diagnosing choice, and it yields consistent estimates of local average effect of diagnosing depression on health outcome for a subset of patients whose diagnosing choice is affected by the instruments selected. The expected value of β_1 is as follows:

(15) $E_{IV}(\beta_1) = \iota_{20} + \iota_{21} * E[A|D(I)]$

E [A|D (I)] is the average unmeasured confounders for marginal patients whose depression diagnosis varies by instruments specified, local area practice styles of diagnosing depression or individual physician preferences to depression diagnosis. If depression was under-diagnosed among AMI patients, diagnosing depression was expected to improve survival and decrease healthcare cost/utilization. Given the concept of treatment-effect heterogeneity and its application to the notion that the effect of depression diagnosing is heterogeneous across patients, IV estimates may reflect the effect of diagnosing for patients on the extensive margin whose diagnosing choice made by physicians would change if overall diagnosing rates changed. It has been argued that patients on the extensive margin and those whose diagnosing decision is affected by instruments may be both drawn from a large sample of patients whose diagnosis is most uncertain.[92, 94, 97, 113, 114, 192]

To test the strength of the relationship between instruments and depression diagnosis, Chow F-test was used to examine whether the instruments describe a statistically significant portion of the variation in depression diagnosis.[213] A rule of

thumb for a strong relationship is the Chow F-value greater than 10. To indirectly assess the relationship between instruments and unmeasured confounders, the Hansen over-identification test was used to examine whether excluding instruments from the second stage of 2SLS is appropriate.[214] A small value of the Hansen statistic indicates little relationship between the instruments and unmeasured confounders.

For the binary outcome variable of 1-year survival, we also employed 2-stage residual inclusion (2SRI) models to estimate the effects of depression diagnosis and test the robustness of our IV estimates.[215]

Aim 2

When Aim 1 was accomplished, we had RA estimates of the average effects of depression diagnosing and IV estimates of the local average effects of depression diagnosing on outcomes. Interpreting the two sets of estimates relies on the assumptions underlying the estimation models. We obtained a convenience sample of the AMI patients in 2007-2008 using chart abstraction from patients. Patients were sampled based upon (1) observed treatment choices of combinations of angiotensin converting enzyme inhibitors/angiotensin receptor blockers, beta blockers, and statins and (2) the values of area treatment ratios of the cardiovascular drug combinations. The chart abstraction data provided important information on patient overall health measured by adult comorbidity evaluation (ACE)-27[216], existing mental illnesses, AMI severity score based on expert opinions and difficulty with activities of daily living (ADLs) [217]. Using the chart abstraction data for a subset of patients, we obtained information on the unmeasured factors in the CCW Medicare claims data that are theoretically related to depression diagnosing decision and outcomes. Depression severity is theorized to be modified by physical function, overall health, and contextual factors (measured in Aim 1). In the chart abstraction data, we captured patient overall health through measures of ACE-27, AMI severity score, and mental illnesses during the index AMI hospitalization. Patient physical function was assessed by ADLs.

The goal of Aim 2 is to assess the assumptions underlying each estimation method. The chart abstraction data on unmeasured factors in Medicare claims data were used to assist in testing the underlying assumption for the RA estimates and ascertain bounds on the true diagnosing effects for patients diagnosed with depression. The unmeasured confounders of physical function and overall health in Medicare claims but measured in chart abstraction were compared across the subset of patients grouped by depression diagnosis and local area depression diagnosing styles. The RA estimators assume that the unmeasured confounders are evenly distributed across depression diagnosis groups. The mean in each of the measures from chart abstraction were compared across depression diagnosing groups and chi-square tests was used to test if there is statistically significant difference in unmeasured confounders using Medicare claims data between the two groups. Comparison of these important patient characteristics across diagnosis groups would help us describe potential bias direction due to assumption violations when interpreting the RA estimates. For instance, if we find that diagnosing depression is associated with better outcomes (Equation (14) $E_{RA}(\beta_1) > 0$) and that patients with worse overall health and worse physical functioning were more likely to be diagnosed with depression, this suggests that estimates of an increase in survival from depression diagnosing understate the true effect and the RA estimate represents a lower bound on the true average effects of depression diagnosing. In contrast, if patients with better overall health and better physical function were more likely to be diagnosed with depression, this suggests that estimates of an increase in survival from depression diagnosing overstate the true effect and the RA estimate represents a higher bound on the true average effects of depression diagnosing.

The IV estimators assume that the unmeasured confounders are evenly distributed across AMI patients grouped by instruments. We used chart abstraction data to test the underlying assumption for the IV estimates and ascertain bounds on the true diagnosing effects for patients whose depression diagnosis is affected by local area depression

diagnosing styles. The mean in each of the measures from hospital charts were compared across patients grouped by ADRs and Armitage trend tests were used to test if there is a statistically significant trend in unmeasured confounders using Medicare claims data among high and low depression diagnosing groups. The comparison results across ADR groups would assist us in describing potential bias direction due to assumption violations when interpreting the IV estimates. For instance, if we find that diagnosing depression is associated with better outcomes in the IV model (Equation (15) $E_{IV}(\beta_1) > 0$) and that patients with worse overall health and worse physical function were more likely to reside in areas with more depression diagnoses, this suggests that estimates of an increase in survival from increasing depression diagnosing rates understate the true effect and the IV estimate represents a lower bound on the true local average effects of depression diagnosing. In contrast, if patients with better overall health and better physical function were more likely to reside in areas with more depression diagnoses, this suggests that estimates of an increase in survival from increasing depression diagnosing rates overstate the true effect and the IV estimate represents a higher bound on the true local average effects of depression diagnosing. The comparison was also conducted for the alternative instruments measured by individual physician practice styles of depression diagnosis to examine the assumptions underlying the IV estimators.

Table 4.1. Depression diagnosis measures

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Depression diagnosis (D)		Yes	Binary variable: 1 if ICD 9 codes are in any of the three depression categories below; 0 otherwise
	Major depressive disorder (MDD)		ICD 9 codes: 296.2x or 296.3x
	Dysthymia		ICD 9 codes: 300.4
	Depressive disorder, not otherwise specified (NOS)		ICD 9 codes: 311

Table 4.2. Outcome measures

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Health outcomes (H)	One-year survival	Yes	Binary variable: 1 if the patient was alive within one year post index date; 0 otherwise
	One-year healthcare cost	Yes	Continuous variable: sum of standardized Medicare payments within one year post index AMI admission
	Part A	Yes	Continuous variable: sum of standardized Medicare Part A payments within one year post index AMI admission
	Part B	Yes	Continuous variable: sum of standardized Medicare Part B payments within one year post index AMI admission
	Outpatient	Yes	Continuous variable: sum of standardized Medicare Part B outpatient payments within one year post index AMI admission
	Physician fee schedule	Yes	Continuous variable: sum of standardized Medicare Part B carrier (physician only) payments within one year post index AMI admission
	Other Part B	Yes	Continuous variable: sum of other standardized Medicare Part B payments within one year post index AMI admission
	Part D	Yes	Continuous variable: sum of standardized Medicare Part D payments within one year post index AMI admission
	One-year healthcare utilization		
	Hospitalizations	Yes	Continuous variable: sum of number of Medicare Part A inpatient claims within one year post index AMI admission

Table 4.2. continued

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Health outcomes (H) (continued)	One-year healthcare utilization (continued)		
	Emergency department (ED) visits	Yes	Continuous variable: sum of number of Medicare Part A inpatient claims and Part B outpatient claims (emergency rooms only) within one year post index AMI admission
	Outpatient visits	Yes	Continuous variable: sum of number of Medicare Part B outpatient claims within one year post index AMI admission
	Physician visits	Yes	Continuous variable: sum of number of Medicare Part B carrier claims (physician office visits of evaluation and management only) within one year post index AMI admission
	Prescription claims	Yes	Continuous variable: sum of number of Medicare Part D prescription claims within one year post index AMI admission

Table 4.3. Measures of control variables

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Depression severity (S)		Not well measured	ICD-9 codes
Physical function (F)		No	
Overall Health (O)		No	
Contextual factors (C)	**Climate**		
	Average annual precipitation by state	Yes	4 binary variables based on precipitation distribution across states
	Average annual temperature by state	Yes	4 binary variables based on temperature distribution across states
	Average annual length of sunlight by state	Yes	4 binary variables based on sunlight distribution across states
	Neighborhood characteristics		
	Neighborhood socioeconomic disadvantage	Yes	Binary variables based on distributions of high school degrees and income across ZIP codes
	Neighborhood poverty level	Yes	Binary variable based on distribution of poverty level across ZIP codes
	Neighborhood problems	Yes	Binary variable based on distribution of crime rates across counties
	Neighborhood walkability	Yes	Binary variable based on distribution of proportion of people walking to work across ZIP codes

Table 4.3. continued

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Contextual factors (C) (continued)	**Neighborhood characteristics (continued)**		
	Residential mobility	Yes	Binary variable based on distribution of proportions of people living in the household for less than 5 years across ZIP codes
	Urban living	Yes	Binary variable
Other factors affecting health outcomes (X)	**Demographics**		
	Age	Yes	4 binary variables indicates age categories
	Gender	Yes	Binary variable
	Race/ethnicity	Yes	6 binary variables indicates race/ethnicity categories
	Low income subsidy	Yes	Binary variable
	Pre-index therapy/procedures		
	Psychotherapy	Yes	Binary variable
	Stent	Yes	Binary variable
	Percutaneous coronary intervention	Yes	Binary variable
	Pace marker implant	Yes	Binary variable
	Coronary artery bypass graft surgery	Yes	Binary variable
	Pre-index medication use		
	Selective serotonin reuptake inhibitors	Yes	Binary variable
	Selective-norepinephrine reuptake inhibitor	Yes	Binary variable
	Tricyclic antidepressants	Yes	Binary variable
	Other antidepressants	Yes	Binary variable

Table 4.3. continued

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Other factors affecting health outcomes (X) (continued)	**Pre-index medication use (continued)**		
	Angiotensin converting enzyme inhibitors	Yes	Binary variable
	Angiotensin receptor blockers	Yes	Binary variable
	Beta blockers	Yes	Binary variable
	Calcium channel blockers	Yes	Binary variable
	Statins	Yes	Binary variable
	Clopidogrel	Yes	Binary variable
	Diuretics	Yes	Binary variable
	Nitrates	Yes	Binary variable
	Pre-index medical conditions		
	Charlson comorbidity index	Yes	Continuous variable
	Anxiety	Yes	Binary variable
	Dementia	Yes	Binary variable
	Bipolar disorders	Yes	Binary variable
	Schizophrenia	Yes	Binary variable
	Substance use disorders	Yes	Binary variable
	Unstable angina	Yes	Binary variable
	Cardiac arrest	Yes	Binary variable
	Ventricular arrhythmias	Yes	Binary variable
	Other cardiac arrhythmias	Yes	Binary variable
	Atrial fibrillation	Yes	Binary variable
	Stroke	Yes	Binary variable
	Transient ischemic attack	Yes	Binary variable
	Ischemic heart disease	Yes	Binary variable
	Heart failure	Yes	Binary variable
	Hypertension	Yes	Binary variable
	Meta solid tumor	Yes	Binary variable
	Any malignancy tumor	Yes	Binary variable
	Hyperlipidemia	Yes	Binary variable
	Chronic kidney disease	Yes	Binary variable

Table 4.3. continued

Model concepts	**Concept measures**	**Measured in this study**	**Description**
Other factors affecting health outcomes (X) (continued)	**Pre-index medical conditions (continued)**		
	Diabetes	Yes	Binary variable
	Chronic obstructive pulmonary disease	Yes	Binary variable
	Asthma	Yes	Binary variable

Note:

Using CCW data from Medicare Part A, B, and D, depression severity, physical function, and overall health were unmeasured or not well measured, but other factors affecting patient health outcomes including patient contextual factors of urban living, demographic characteristics, healthcare service use, and medical conditions were measured;

Using National Weather Service data, contextual factors of climate on precipitation, temperatures, and sunlight were measured;

Using Federal Bureau of Investigation (FBI) Uniform Crime Reports (UCR) and United States Census Data, contextual factors on neighborhood characteristics were measured. Neighborhood problems regarding traffic and noise were very specific and self-reported measures in previous studies.[218, 219] In this study, urban living served as a proxy measure to capture these neighborhood problems;

Pre-index medical conditions and therapy/procedures were measured in the previous 12 months before the index AMI admission;

Pre-index medication use was measured in the previous 6 months before the index AMI admission. Other antidepressants included bupropion, traZODONE, maprotiline, isocarboxazid, phenelzine, tranylcypromine, selegiline, nefazodone, mirtazapine, St. John's wort, and 5-hydroxytryptophan.

CHAPTER V

RESULTS

Aim 1

Study sample

There were 639,819 Medicare beneficiaries newly hospitalized with AMI in 2007 and 2008 (Table 5.1). After the inclusion criteria were applied, the final study sample was restricted to 155,841 patients for outcome assessment associated with depression diagnosis within 30 days post the index AMI admission, 149,989 patients to assess depression diagnosis within 60 days post the index AMI admission, and 145,567 patients to assess depression diagnosis within 90 days post the index AMI admission.

Compared with patients who were excluded from our study, those in the analytical sample with 30-day observation window tended to be younger, Hispanic, Asian, and female (Table 5.2). In addition, only 69.5% of the Medicare beneficiaries included in our analyses lived in metropolitan areas, yet 74.5% of the excluded sample did. Patients in the analytical sample were also more likely to live in areas with fewer neighborhood problems, higher walkability, less residential mobility, and more socioeconomic disadvantage in terms of income, poverty, and education. Lastly, there were more patients in the analytical sample residing in areas with more sunshine, higher temperature, and more precipitation.

Descriptive statistics of patient characteristics across depression diagnosis groups

Table 5.3 shows that depression diagnosis rates increased with longer observation windows. About 5.9% of the study sample had a depression diagnosis within the first 30 days after the AMI admission. In addition, 7.7% had a depression diagnosis within the first 60 days and 9.1% had a depression diagnosis within the first 90 days after the index AMI admission.

Because estimates of the effects of depression diagnosis on healthcare utilization and costs were reported across different observation windows, we compared the patients diagnosed with depression within 30 days after the index AMI admission to those who were first diagnosed in the periods of 30-60 and 60-90 days after admission (Table 5.4). We found 9199 patients diagnosed with depression within 30 days after the index AMI admission, 2894 diagnosed during the 30-60 days, and 2166 diagnosed during the 60-90 days post the index AMI admission. Compared with patients diagnosed with depression within 30 days after the index AMI admission, those diagnosed later were more likely to be black, Hispanic, and male. In addition, these patients diagnosed within 30-90 days after the index AMI admission tended to have less bipolar disorders and Alzheimer's disease, but more other medical conditions during the 12 months prior the index AMI admission. Compared with patients diagnosed within 30 days after the index AMI admission, those diagnosed in the later periods were less likely to have psychotherapy during the 12 months prior the index AMI admission or antidepressants during the 6 months prior admission, but more likely to have other medications during the 6 months prior admission. Those patients diagnosed later also tended to live in areas with higher poverty, lower education, and higher temperature. Lastly, patients diagnosed in the later periods had relatively lower 1-year survival rates than those diagnosed in the first 30 days post the index AMI admission date. They were more likely to have higher total healthcare costs, Part A and B costs, total Part B costs and outpatient, physician fee schedule, and other costs over the 1-year period post AMI, but had a trend to have fewer prescription claims.

Compared with undiagnosed patients with depression within 30 days after the index AMI admission, the diagnosed patients were more likely to be older, white, and female, but less likely to have low income subsidy (Table 5.5). For medical conditions 12-month prior the index AMI admission, the patients diagnosed with depression were also more likely to have other mental illnesses (anxiety, bipolar disorder, schizophrenia,

Alzheimer, and substance use disorder), stroke, hypertension, and chronic obstructive pulmonary disease, yet less likely to have unstable angina, ventricular arrhythmia, ischemic heart disease, hyperlipidemia, chronic kidney disease, and diabetes. In addition, the diagnosed patients tended to receive less procedures 12-month prior the index AMI admission, including coronary artery bypass grafting, percutaneous coronary intervention, and stent. Furthermore, patients diagnosed with depression were more likely to have psychotherapy 12-month and antidepressants 6-month prior the index AMI admission. The diagnosed patients tended to live in metropolitan areas and areas with higher income, lower poverty, and higher education measured by 2000 United States Census data. Also, they were more likely to reside in areas with less sunshine, lower temperature, and higher precipitation using National Weather Service data in 2007-2008. Similar distributions of patient characteristics across depression diagnosis groups were found for the other two analytical samples with longer observation windows.

Lastly, diagnosed patients were less likely to survive or to have higher outpatient costs in the first year post the index AMI admission date, but more likely to have higher total healthcare cost, Part A and D costs, and higher utilizations of hospitalizations, ED visits, physician visits, and prescription claims for patients with 30-day observation window. In the other 2 samples, patients diagnosed with depression were less likely to survive, but more likely to have higher healthcare costs (except Part B outpatient costs) and utilizations for all measures than those without a depression diagnosis.

RA estimates of the effectiveness of depression diagnosis

Unadjusted differences in outcome measures across depression diagnosis groups were generally larger than the adjusted differences, except for total Part B and outpatient costs. After adjusting for patient demographics, pre-index medical conditions, therapy/procedure use, and medication use, and contextual factors, depression diagnosis within 30 days after the index, AMI admission was statistically significantly associated

with decreased 1-year survival and increased one-year healthcare costs for patients diagnosed with depression (Table 5.6). Within the total healthcare costs, depression diagnosis was related to increased Part A costs and Part B outpatient costs for patients diagnosed with depression. In addition, depression diagnosis was associated with increased utilization of hospitalization, ED visits, physician visits, and prescription claims during the first year after the index AMI admission for the diagnosed patients with depression. Consistent estimates of depression diagnosis on outcomes were also found for depression diagnosis measured within 60- and 90-day observation window, but exceptions did occur. For example, depression diagnosis within 90 days after AMI admission was associated with increased Part B physician fee schedule cost, other Part B cost, Part D cost and outpatient visits.

Area diagnosis ratios (ADRs) as instruments

Variation in patient characteristics across ADR-based instrument groups

One of the instruments in the IV analysis, based on local area depression diagnosing styles analysis, was measured by adjusted area depression diagnosis ratios. Moving from the first to the fifth quintile ADR-based groups, depression diagnosis rates within 30 days after the index AMI admission varied from 3.2% to 9.0% (Table 5.7). Variation in patient characteristics across patients grouped by the ADR-based instruments was generally smaller than across depression diagnosis groups, but exceptions did occur. For example, patients in a higher ADR quintile group were more likely to have other cardiac arrhythmia and atrial fibrillation than those in a lower ADR group. In addition, these patients in a higher ADR quintile group were more likely to be Hispanic and to have β-blockers or ARBs 6-month prior the index AMI admission, but less likely to have diuretics 6-month prior admission. For the 1-year outcomes, patients in a higher ADR quintile group were more likely to have higher 1-year total healthcare costs, Part A, B

(mostly from physician fee schedule cost), and D costs and more physician visits. Other measures of 1-year outcomes were evenly distributed across ADR quintile groups.

Strength of instrument with depression diagnosis

One assumption underlying IV estimators is that the instrument is strongly related to the treatment decision. Therefore, we performed Chow test F-statistic to assess the strength of ADR-based instruments with depression diagnosis decision in the first stage of 2SLS.[213] With local area sizes varying from 50 to 200 persons, Chow-F values changed from 765 to 235 for depression diagnosis within 30 days after the index AMI admission (Table 5.8). For example, in the 150-person area with patients grouped into ADR-based quintile groups, the Chow-F value was 286, which suggested that our ADR-based instruments described a significant portion of variation in depression diagnosis (Chow-F value > 10).[220] Consistent Chow-F values were found for modeling depression diagnosis within 60 and 90 days after the index AMI admission.

Figure 5.1a-c shows the northeastern maps of the 5-digit ZIP code level variation in practice styles of depression diagnosis as measured by DACC-based ADRs. The darker color indicated higher ADRs for depression diagnosis. The maps illustrated that the DACC method captured substantial variation in depression diagnosis styles across small areas and relatively high and low practice style ZIP codes spread out across the country.

IV estimates of the effectiveness of depression diagnosis

Unadjusted differences in 1-year outcome measures across the ADR-based instrument groups were generally larger than the adjusted differences in IV estimation for samples with 30- and 60-day observation windows. However, in the sample with 90-day observation window, unadjusted differences in 1-year total healthcare cost, Part A and B costs were smaller than the IV estimates. The IV analysis shows that higher depression diagnosis rates in the 30-day observation window had a positive relationship with the one-year total healthcare costs, Part A, B (mostly from physician fee schedule and other

Part B costs) and D costs for marginal patients whose depression diagnosis was affected by the ADR-based instruments (Table 5.9). In terms of healthcare utilization, increasing depression diagnosis rates within 30 days after the index AMI admission was associated with increased Part B physician visits, but it was associated with decreased ED visits and prescription claims in 1 year for the marginal patients. No statistically significant relationship was found between depression diagnosis and 1-year survival.

Higher rates of depression diagnosis within 60 days after the index AMI admission were also associated with marginally decreased 1-year survival rates, but statistically significantly increased 1-year total healthcare costs and Part A and B costs including, outpatient, physician fee schedule, and other Part B costs for the marginal patients. For healthcare utilization, increased depression diagnosis rates within 60 days after the index AMI admission had statistically significant relationships with increased hospitalizations and physician visits, but decreased prescription claims for the marginal patients. Only marginal effect was shown between increased depression diagnosis rates and decreased ED visits. Higher rates of depression diagnosis rates within 90 days after the index AMI admission were associated with increased healthcare costs in all measures, increased hospitalizations and physician visits, but fewer prescription claims in 1 year. However, no statistically significant relationship was found between depression diagnosis and other 1-year outcomes in samples with 60/90 days observation windows.

The Hansen[214] over-identification F tests in the second stage of the IV analyses were not statistically significant for most outcome measures, indicating that the ADR-based instruments did not have a direct effect on these outcomes. However, using prescription drug claims as an outcome measure, the ADR instruments in the 30-day observation window indicated direct relationships. This means that interpretation of these outcomes requires caution. In the 60-day observation window, the ADR-based instruments suggested direct relationships with hospitalizations, ED visits, and outpatient

visits. In the 90-day observation window, a relationship was only found between depression diagnosis and outpatient visits.

Sensitivity analyses showed that IV estimates of depression diagnosis on outcomes among elderly patients with AMI were consistent in terms of magnitude and statistical significance across the variety of instrument specifications employed (Table A1-39). With standard errors clustered on ZIP code level, we found consistent Chow F values and IV estimates in terms of magnitude and statistical significance with our main results presented here. In addition, our 2SRI estimators yielded consistent estimates of depression diagnosis on 1-year survival with 2SLS estimators (Table A40-42).

Furthermore, similar results were found for the cleaner sample of patients without bipolar disorder, psychotherapy, and antidepressant use prior to the index AMI admission (Table A43). However, by excluding the patient from his/her own ADR calculation, the first stage Chow F values decreased substantially to 17-26 for 150-person local areas (Table A44). Chow F values great than 10 suggested that our instrument of local area depression diagnosis styles described a large portion of variation in depression diagnosis, but much smaller variation was explained than including the patient for his/her own ADR calculation (284-289 for Chow F values). Depression diagnosis rates within 30 days after AMI admission only varied from 5.5% to 6.7% from the 1^{st} to the 5^{th} ADR quintile groups. IV estimates using the ADR-based instrument by excluding the patient from his/her own ADR calculation showed that higher depression diagnosis rates were associated with higher healthcare costs and utilization for patients whose depression diagnosis was affected by this instrument. These results were consistent in terms of statistical significance and directions with our main results presented in Table 5.9 and Table A1-39, but generally larger regarding magnitude than the main results. Using unadjusted area depression diagnosis rates and excluding the patient from his/her area rate calculation, similar results were found for using ADR-based instruments and excluding that patient (Table A45). With little variation in depression diagnosis rates to

be exploited across ADR quintile groups and much smaller Chow F values, the much weaker instruments by excluding the patient from his/her own ADR or unadjusted area rate calculation might lead to biased estimates of the effects of depression diagnosis on patient outcomes.

Individual physician practice styles as instruments

Variation in patient characteristics across patients grouped by individual physician depression diagnosis rates (prior 6 months)

Depression diagnosis rate was 5.5% for patients seeing physicians who did not give a depression diagnosis in the previous 6 months of the index AMI admission and it was 10.9% for patients seeing physicians who did (Table 5.10). Variation in patient characteristics across patients grouped by the individual practice style-based instruments was generally similar to or greater than across depression diagnosis groups. This suggested that similar patterns might exist among patient characteristics in unmeasured ways. In terms of 1-year outcome measures, patients seeing physicians who gave depression diagnoses in the previous 6 months of the index AMI admission were less likely to survive, but more likely to have higher healthcare costs and utilization in all measures, except Part D cost. Therefore, instruments based on the measure of individual practice styles might not be valid and interpretation of the IV estimates based upon this instrument measures requires caution.

Strength of instruments with depression diagnosis

In IV analysis, one assumption is that the instrument is strongly related to the treatment decision. Therefore, Chow test F-statistic was performed to examine the strength of physician prior depression diagnosis rates-based instruments with depression diagnosis decision in the first stage of 2SLS. The Chow-F values ranged from 305 to 526 for depression diagnosis within 30 to 90 days after the index AMI admission (Table 5.11). All our Chow F-values > 10 suggested that the physician prior depression

diagnosis rates-based instruments described a significant portion of variation in depression diagnosis.

IV estimates of

the effectiveness of depression diagnosis

Unadjusted differences in 1-year outcome measures across patients grouped by individual physician prior depression diagnosis rates were generally larger than the adjusted differences in IV estimation. IV analysis showed that higher depression diagnosis rates within 30 days after the index AMI admission were associated with lower 1-year survival rates, higher total healthcare costs, Part A and B costs (total Part B, outpatient, and physician fee schedule cost) for the marginal patients whose depression diagnosis was affected by the instrument specified (Table 5.12). In terms of healthcare utilization, increasing depression diagnosis rates was associated with increased hospitalizations, ED visits, outpatient visits, and physician visits for the marginal patients. No statistically significant relationships were found between depression diagnosis and Part D cost or the number of prescription claims. No over-identification tests were conducted, because the number of instruments (a binary variable of individual physician diagnosis rates) equals the number of endogenous variables (a binary variable of depression diagnosis).

Similar patterns on healthcare costs were found for depression diagnosis measured in 60 and 90 days. Additionally, higher rates of depression diagnosis within 60 or 90 days after AMI admission also had statistically significant positive relationships with the number of prescription claims in 1 year.

Aim 2

Among patients with 30-day observation window, 72 out of a convenience sample of 1403 patients had a depression diagnosis within 30 days after the index AMI admission. Even though the differences across the diagnosis or instrument groups were not statistically significant, Table 5.13 shows that patients diagnosed with depression

within 30 days after the index AMI admission were more likely to use walkers and have other unspecified difficulties of daily living, but less likely to have problems with dressing/undressing, feeding oneself, or incontinence/elimination. They were also more likely to have moderate comorbidity measured by ACE-27. Furthermore, the diagnosed patients were more likely to have depression or bipolar disorder, dementia, or other mental illness recorded in hospital chart during the index AMI hospitalization.

Across the ADR-based instruments groups, most of these measures in hospital charts were more evenly distributed than across depression diagnosis groups, which suggested our instruments did not have a direct relationship with unmeasured confounders (Table 5.14). However, patients in a higher ADR quintile group tended to have increased incontinence/elimination difficulties and to use a wheelchair. Thus, our IV estimates of the effects of depression diagnosis on 1-year outcomes might be biased toward lower survival rates and higher healthcare costs and utilization.

Grouped by individual physician diagnosis rates, patients who visited physicians diagnosing depression 6-month prior to the index AMI admission were more likely to have difficulties with activities of daily living including personal hygiene/grooming, use of a cane, walker or wheelchair, and having bed bound, but less likely to have problems with feeding oneself or incontinence/elimination (Table 5.15). Furthermore, they tended to have moderate or severe comorbidity measured by ACE-27 and dementia, but not to have depression/bipolar disorder, alcohol abuse, or other mental illnesses. This suggested that the instruments based on individual practice styles might not be valid and the IV estimates based on the instruments might be biased toward lower survival rates and higher healthcare costs and utilization.

Table 5.1. Inclusion criteria for the analytical sample

Criteria	**30-day observation window**	**60-day observation window**	**90-day observation window**
AMI admissions in 2007 and 2008 (no AMI admissions prior 12 months)	639819		
Survived at discharge	545871		
Lower 48 states	540451		
Discharged in 2007 and 2008	538459		
Institutionalized < 100 days	538120		
Age 66 +	457714		
No HMO prior 12 months of AMI admission	428538		
Part A & B prior 12 months of AMI admission	414940		
Part D prior 6 months of AMI admission	204070		
No HMO within 12 months after of AMI admission	197550		
Part A & B within 12 months after of AMI admission	194719		
Part D later within 12 months after of AMI admission	192620		
No hospice prior 12 months of AMI admission	188023		
Survived the first 30/60/90 days after AMI admission	184249	176764	171090
With driving information between ZIPs*	184201	176717	171045
No depression diagnosis prior 12 months	**155841**	**149989**	**145567**

Notes:

*Driving information between ZIPs in the United States was obtained from Microsoft MapPoint 2010;
AMI (acute myocardial infarction);
HMO (health maintenance organization).

Table 5.2. Descriptive statistics between the analytical sample (30-day observation window) and the excluded sample

Variables	**Excluded sample**	**Analytical sample**	**Chi-square test (P value)**	**Total (%)**
Sample size	**483978**	**155841**		**639819**
Demographics				
Age				
66-70	13.5	18.6	<0.0001*	94395(14.8%)
71-75	14.3	18.9	<0.0001*	98821(15.4%)
76-80	16.3	20.3	<0.0001*	110335(17.2%)
81-85	16.9	19.2	<0.0001*	111714(17.5%)
85+	20.6	23.1	<0.0001*	135542(21.2%)
Race				
White	83.4	82.5	<0.0001*	532136(83.2%)
Black	8.8	8.6	0.0152*	55779(8.7%)
Hispanic	5.1	5.7	<0.0001*	33291(5.2%)
Asian	1.2	2.0	<0.0001*	9013(1.4%)
American native	0.5	0.5	0.6873	3222(0.5%)
Other race	0.6	0.5	<0.0001*	3821(0.6%)
Unknown race	0.4	0.2	<0.0001*	2096(0.3%)
Female	46.5	57.1	<0.0001*	313882(49.1%)
Contextual factors				
Urban living				
Metropolitan	74.5	69.5	<0.0001*	468828(73.3%)
Non-metropolitan	24.6	30.5	<0.0001*	166526(26%)
Unknown	0.9	0.0	<0.0001*	4465(0.7%)
Neighborhood problems				
Above median crime rate	59.0	54.5	<0.0001*	370385(57.9%)
Missing crime rate	27.9	29.6	<0.0001*	181364(28.3%)
Walkability				
Above median walkability	43.4	47.0	<0.0001*	377342(59%)
Missing walkability	0.3	0.1	<0.0001*	308306(48.2%)
Residential mobility			<0.0001*	334220(52.2%)
Above median residence (5+ years)	71.0	70.1	<0.0001*	1608(0.3%)
Missing residence	0.3	0.1		

Table 5.2 Continued

Variables	Excluded sample	Analytical sample	Chi-square test (P value)	Total (%)
Contextual factors (continued)				
Socioeconomic disadvantage			<0.0001*	283426(44.3%)
Above median income	59.9	56.0	<0.0001*	1671(0.3%)
Above median poverty	47.3	50.9		
Above median high school degrees	53.1	49.4	<0.0001*	452746(70.8%)
Missing socioeconomics	0.3	0.0	<0.0001*	1665(0.3%)
Climate				
Above median sunshine	43.4	45.4	<0.0001*	280639(43.9%)
Above median temperature	62.2	64.1	<0.0001*	401027(62.7%)
Above median precipitation	34.6	37.2	<0.0001*	225420(35.2%)

Notes:

Chi-square test was used to examine differences in characteristic value across patients in the analytical and excluded samples. For example, the p value for anxiety tests whether the difference in female rates exists across the two groups; *significant at 95% CI.

Table 5.3. Depression diagnosis for elderly patients with acute myocardial infarction

Samples	**Sample size**	**# of patients diagnosed with depression (%)**
30-day observation window	155841	9199(5.9%)
60-day observation window	149989	11598(7.7%)
90-day observation window	145567	13175(9.1%)

Table 5.4. Patient characteristics across patients diagnosed with depression in varying observation windows (Medicare claims-elderly patients with acute myocardial infarction)

Variables	**Patients diagnosed with depression within 30 days after AMI admission**	**Patients diagnosed with depression within 30-60 days after AMI admission**	**Patients diagnosed with depression within 60-90 days after AMI admission**	**Chi-square test**	**Total (%)**
n	**9199**	**2894**	**2166**		**14259**
Demographics					
Age					
66-70	17.2	16.2	16.5	0.2823	2407(16.9%)
71-75	16.0	18.1	16.9	0.0693	2362(16.6%)
76-80	19.3	21.4	20.9	0.0206*	2847(20%)
81-85	21.1	20.8	21.2	0.9930	3002(21.1%)
85+	26.4	23.5	24.5	0.0062*	3641(25.5%)
Race					
White	87.7	84.2	84.9	<0.0001*	12343(86.6%)
Black	5.2	7.3	6.8	<0.0001*	832(5.8%)
Hispanic	5.0	5.9	6.1	0.0139*	767(5.4%)
Asian	1.2	1.6	1.0	0.6707	180(1.3%)
American native	0.4	0.4	0.3	0.6562	50(0.4%)
Other race	0.3	0.4	0.7	0.0258*	58(0.4%)
Unknown race	0.2	0.2	0.2	0.9395	29(0.2%)
Female	69.6	65.1	67.0	0.0003*	9736(68.3%)
Low income subsidy	5.8	5.8	6.0	0.8332	830(5.8%)

Table 5.4 Continued

Variables	Patients diagnosed with depression within 30 days after AMI admission	Patients diagnosed with depression within 30-60 days after AMI admission	Patients diagnosed with depression within 60-90 days after AMI admission	Chi-square test	Total (%)
Pre-index medical conditions					
Charlson comorbidity scores					
0	32.3	26.8	27.7	<0.0001*	4345(30.5%)
1	23.9	23.0	23.4	0.4068	3373(23.7%)
2	15.5	14.9	15.7	0.9656	2199(15.4%)
3	11.4	11.7	11.4	0.8337	1634(11.5%)
4+	16.9	23.6	21.7	<0.0001*	2708(19%)
Mental illnesses					
Anxiety	12.7	12.0	12.3	0.4528	1784(12.5%)
Bipolar disorder	1.8	1.5	1.2	0.0413*	235(1.6%)
Schizophrenia	1.3	0.9	0.9	0.0986	163(1.1%)
Alzheimer's disease	18.7	15.0	15.1	<0.0001*	2484(17.4%)
Substance use disorder	1.6	1.9	1.9	0.1850	246(1.7%)
Unstable angina	7.5	9.6	9.1	0.0006*	1166(8.2%)
Cardiac Arrest	0.4	0.4	0.3	0.8025	54(0.4%)
Ventricular Arrhythmia	2.4	2.9	4.2	<0.0001*	398(2.8%)
Other cardiac arrhythmia	32.9	36.7	35.1	0.0028*	4849(34%)
Atrial fibrillation	13.8	15.0	14.4	0.2086	2011(14.1%)
Stroke	6.5	7.3	7.2	0.1275	963(6.8%)
Ischemic heart disease	53.5	58.5	57.8	<0.0001*	7864(55.2%)
Heart failure	33.0	38.6	37.3	<0.0001*	4963(34.8%)

Table 5.4 Continued

Variables	Patients diagnosed with depression within 30 days after AMI admission	Patients diagnosed with depression within 30-60 days after AMI admission	Patients diagnosed with depression within 60-90 days after AMI admission	Chi-square test	Total (%)
Pre-index medical conditions (continued)					
Transient ischemic attack	1.8	2.5	2.4	0.0284*	291(2%)
Hyperlipidemia	62.0	65.6	65.1	0.0004*	9015(63.2%)
Hypertension (complicated)	6.6	6.9	6.7	0.6506	953(6.7%)
Hypertension (uncomplicated)	82.4	85.0	86.0	<0.0001*	11897(83.4%)
Chronic kidney disease	16.7	22.7	21.2	<0.0001*	2655(18.6%)
Diabetes	36.5	42.3	41.4	<0.0001*	5484(38.5%)
Chronic obstructive pulmonary disease	28.4	31.9	31.4	0.0002*	4212(29.5%)
Asthma	7.4	7.8	6.8	0.6170	1051(7.4%)
Any malignancy	9.1	9.7	10.3	0.0567	1341(9.4%)
Meta solid tumor	1.9	2.2	2.2	0.3767	288(2%)
Pre-index therapy/procedures					
Psychotherapy	2.1	1.3	1.2	0.0011*	260(1.8%)
Coronary artery bypass grafting	0.3	0.6	0.3	0.5613	53(0.4%)
Percutaneous coronary intervention	0.6	0.8	0.8	0.0819	92(0.6%)
Pacemaker implant	0.9	1.1	0.6	0.3137	125(0.9%)
Stent	1.9	2.6	2.4	0.0621	304(2.1%)

Table 5.4 Continued

Variables	Patients diagnosed with depression within 30 days after AMI admission	Patients diagnosed with depression within 30-60 days after AMI admission	Patients diagnosed with depression within 60-90 days after AMI admission	Chi-square test	Total (%)
Pre-index medication use					
Antidepressants					
SSRIs	38.8	23.4	22.4	<0.0001*	4731(33.2%)
SNRIs	6.2	3.4	3.3	<0.0001*	742(5.2%)
TCAs	6.1	4.8	4.7	0.0014*	800(5.6%)
Other antidepressants	10.7	6.5	6.8	<0.0001*	1317(9.2%)
ACE inhibitors	35.9	38.1	36.9	0.1489	5208(36.5%)
ARBs	18.1	18.9	20.6	0.0093*	2660(18.7%)
β-blcokers	47.9	49.2	49.6	0.0945	6906(48.4%)
CCBs	30.8	32.2	31.0	0.5043	4437(31.1%)
Clopidogrel	16.3	18.9	19.0	0.0002*	2457(17.2%)
Diuretics	50.8	53.7	55.6	<0.0001*	7434(52.1%)
Nitrates	22.8	25.0	23.4	0.1704	3324(23.3%)
Statins	40.7	43.2	42.9	0.0125*	5921(41.5%)
Contextual factors					
Urban living					
Metropolitan	71.5	74.5	72.2	0.0957	10298(72.2%)
Non-metropolitan	28.5	25.3	27.8	0.0933	3952(27.7%)
Unknown	0.0	0.2	0.0	0.8440	9(0.1%)
Neighborhood problems					
Above median crime rate	53.4	54.5	54.2	0.3135	7661(53.7%)
Missing crime rate	30.9	31.3	30.7	0.9730	4417(31%)

Table 5.4 Continued

Variables	Patients diagnosed with depression within 30 days after AMI admission	Patients diagnosed with depression within 30-60 days after AMI admission	Patients diagnosed with depression within 60-90 days after AMI admission	Chi-square test	Total (%)
Contextual factors (continued)					
Walkability					
Above median walkability	47.6	47.8	47.1	0.7453	6785(47.6%)
Missing walkability	0.1	0.1	0.0	0.4318	7(0%)
Residential mobility					
Above median residence (5+ years)	70.8	70.9	71.1	0.7827	10101(70.8%)
Missing residence	0.1	0.0	0.0	0.1956	7(0%)
Socioeconomic disadvantage					
Above median income	59.1	59.3	56.0	0.0235*	8365(58.7%)
Above median poverty	47.9	49.0	51.8	0.0013*	6947(48.7%)
Above median high school degrees	53.3	52.0	49.5	0.0013*	7484(52.5%)
Missing socioeconomics	0.0	0.0	0.0	0.3566	5(0%)
Climate					
Above median sunshine	42.7	41.8	43.5	0.7349	6076(42.6%)
Above median temperature	60.8	61.5	64.5	0.0023*	8772(61.5%)
Above median precipitation	40.0	38.9	39.6	0.5148	5662(39.7%)

Table 5.4 Continued

Variables	Patients diagnosed with depression within 30 days after AMI admission	Patients diagnosed with depression within 30-60 days after AMI admission	Patients diagnosed with depression within 60-90 days after AMI admission	Chi-square test	Total (%)
One-year outcomes					
Survival	72.9	67.4	71.3	0.0014*	10199(71.5%)
Total healthcare cost	20488.1	26048.7	27963.0	<0.0001*	22752.1
Part A	11987.4	16167.9	17257.7	<0.0001*	13636.4
Part B	5669.3	7150.3	7789.0	<0.0001*	6291.9
Outpatient	1716.8	2148.7	2453.4	<0.0001*	1916.3
Physician fee schedule	2595.9	3305.5	3495.8	<0.0001*	2876.6
Others	1356.6	1696.0	1639.8	<0.0001*	1498.9
Part D	2831.4	2730.6	2916.3	0.0701	2823.8
Healthcare utilization					
# of hospitalizations	1.2	1.4	1.2	0.0003*	1.2
# of ED visits	1.6	1.7	1.6	0.2914	1.6
# of outpatient visits	7.0	7.1	6.7	0.2590	7.0
# of physician visits	24.5	26.6	23.9	<0.0001*	24.8
# of prescription claims	61.8	56.3	53.4	<0.0001*	59.4

Notes:

Cochran-Armitage test was used to examine trend in characteristic value across patients diagnosed with depression in varying observation windows. For example, the p value for anxiety tests whether a linear trend in anxiety rates exists across patient groups based on the time period when the first depression diagnosis was made;
*significant at 95% CI;
Pre-index medical conditions and therapy/procedures were measured in the previous 12 months before the index AMI admission;

Table 5.4 Continued

Notes (Continued):

Pre-index medication use was measured in the previous 6 months before the index AMI admission;
SSRI (selective serotonin reuptake inhibitor);
SNRI (selective-norepinephrine reuptake inhibitor);
TCA (tricyclic antidepressants);
Other antidepressants included bupropion, traZODONE, maprotiline, isocarboxazid, phenelzine, tranylcypromine, selegiline, nefazodone, mirtazapine, St. John's wort, and 5-hydroxytryptophan;
ACEI (angiotensin-converting enzyme inhibitor);
ARB (angiotensin II receptor blockers);
Statins (HMG-CoA reductase inhibitors);
ED (emergency department);
Analysis of variance (ANOVA) test was used to examine differences in characteristic value across patients diagnosed with depression in varying observation windows for continuous variables, including all healthcare cost and utilization measures. Means were reported for continuous variables;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;

Table 5.4 Continued

Notes (Continued):

Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.

Table 5.5. Patient characteristics across depression diagnosis groups among elderly patients with acute myocardial infarction (Medicare claims)

	Depression diagnosis within 30 days after AMI admission		Chi-square test	Depression diagnosis within 60 days after AMI admission		Chi-square test	Depression diagnosis within 90 days after AMI admission		Chi-square test
Variables	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**
n	146642	9199	155841	138391	11598	149989	132392	13175	145567
Demographics									
Age									
66-70	18.6	17.2	0.0004*	19.1	17.4	<0.0001*	19.4	17.6	<0.0001*
71-75	19.1	16.0	<0.0001*	19.4	16.7	<0.0001*	19.6	17.1	<0.0001*
76-80	20.3	19.3	0.0155*	20.5	20.0	0.2096	20.6	20.2	0.2546
81-85	19.1	21.1	<0.0001*	18.9	21.0	<0.0001*	18.8	21.0	<0.0001*
85+	22.9	26.4	<0.0001*	22.1	24.8	<0.0001*	21.6	24.1	<0.0001*
Race									
White	82.2	87.7	<0.0001*	82.2	86.8	<0.0001*	82.3	86.4	<0.0001*
Black	8.8	5.2	<0.0001*	8.7	5.6	<0.0001*	8.7	5.8	<0.0001*
Hispanic	5.7	5.0	0.0050*	5.7	5.3	0.0459*	5.7	5.5	0.3115
Asian	2.1	1.2	<0.0001*	2.1	1.3	<0.0001*	2.1	1.3	<0.0001*
American native	0.5	0.4	0.0515	0.5	0.4	0.0495*	0.5	0.4	0.0324*
Other race	0.5	0.3	0.0393*	0.5	0.4	0.0716	0.5	0.4	0.3203
Unknown race	0.2	0.2	0.9993	0.2	0.2	0.4646	0.2	0.2	0.6285
Female	56.3	69.6	<0.0001*	56.0	68.6	<0.0001*	55.8	68.5	<0.0001*
Low income subsidy	6.3	5.8	0.0432*	6.4	5.8	0.0292*	6.4	5.8	0.0156*

Table 5.5 Continued

	Depression diagnosis within 30 days after AMI admission		Chi-square test	Depression diagnosis within 60 days after AMI admission		Chi-square test	Depression diagnosis within 90 days after AMI admission		Chi-square test
Variables	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**
Pre-index medical conditions									
Charlson comorbidity scores									
0	33.6	32.3	0.0071*	34.3	31.4	<0.0001*	34.9	31.2	<0.0001*
1	22.9	23.9	0.0263*	23.1	23.9	0.0409*	23.2	24.1	0.0236*
2	14.3	15.5	0.0012*	14.2	15.2	0.0024*	14.2	15.3	0.0004*
3	10.4	11.4	0.0028*	10.3	11.4	0.0002*	10.2	11.3	<0.0001*
4+	18.7	16.9	<0.0001*	18.1	18.1	0.8938	17.6	18.1	0.1260
Mental illnesses									
Anxiety	6.2	12.7	<0.0001*	6.1	12.6	<0.0001*	5.9	12.7	<0.0001*
Bipolar disorder	0.6	1.8	<0.0001*	0.6	1.7	<0.0001*	0.5	1.6	<0.0001*
Schizophrenia	0.6	1.3	<0.0001*	0.5	1.2	<0.0001*	0.5	1.2	<0.0001*
Alzheimer	10.9	18.7	<0.0001*	10.3	17.3	<0.0001*	9.8	16.7	<0.0001*
Substance use disorder	1.3	1.6	0.0077*	1.3	1.7	<0.0001*	1.2	1.7	<0.0001*
Unstable angina	9.0	7.5	<0.0001*	9.0	8.1	0.0008*	9.0	8.2	0.0025*
Cardiac Arrest	0.4	0.4	0.6894	0.4	0.4	0.6518	0.4	0.4	0.5101
Ventricular Arrhythmia	3.4	2.4	<0.0001*	3.3	2.4	<0.0001*	3.3	2.6	0.0001*
Other cardiac arrhythmia	32.6	32.9	0.5618	32.1	33.3	0.0070*	31.7	33.0	0.0016*
Atrial fibrillation	13.7	13.8	0.8630	13.4	13.8	0.2283	13.1	13.5	0.1864
Stroke	5.3	6.5	<0.0001*	5.1	6.6	<0.0001*	5.0	6.6	<0.0001*
Ischemic heart disease	56.5	53.5	<0.0001*	56.2	54.6	0.0008*	56.0	54.9	0.0108*
Heart failure	32.2	33.0	0.1054	31.3	33.7	<0.0001*	30.6	33.7	<0.0001*
Transient ischemic attack	1.9	1.8	0.8547	1.8	2.0	0.1927	1.8	2.0	0.0252*

Table 5.5 Continued

	Depression diagnosis within 30 days after AMI admission		Chi-square test	Depression diagnosis within 60 days after AMI admission		Chi-square test	Depression diagnosis within 90 days after AMI admission		Chi-square test
Variables	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**
Pre-index medical conditions (continued)									
Hyperlipidemia	65.9	62.0	<0.0001*	66.3	63.2	<0.0001*	66.6	63.8	<0.0001*
Hypertension (complicated)	6.3	6.6	0.2650	6.3	6.7	0.0848	6.3	6.7	0.0279*
Hypertension (uncomplicated)	81.4	82.4	0.0209*	81.2	83.0	<0.0001*	81.0	83.5	<0.0001*
Chronic kidney disease	19.3	16.7	<0.0001*	18.8	18.0	0.0254*	18.4	18.1	0.5016
Diabetes	38.1	36.5	0.0029*	37.9	38.0	0.8836	37.7	38.4	0.1272
Chronic obstructive pulmonary disease	25.8	28.4	<0.0001*	25.3	28.8	<0.0001*	24.9	29.0	<0.0001*
Asthma	7.1	7.4	0.2571	7.1	7.5	0.0795	7.1	7.4	0.1800
Any malignancy	9.1	9.1	0.9066	9.0	9.1	0.6877	8.8	9.1	0.2704
Meta solid tumor	2.1	1.9	0.1851	2.0	1.8	0.1710	1.9	1.8	0.4851
Pre-index therapy/procedures									
Psychotherapy	0.6	2.1	<0.0001*	0.6	2.0	<0.0001*	0.6	1.9	<0.0001*
Coronary artery bypass grafting	0.5	0.3	0.0141*	0.5	0.4	0.1216	0.5	0.4	0.0592
Percutaneous coronary intervention	0.8	0.6	0.0085*	0.8	0.6	0.0470*	0.8	0.7	0.0710
Pacemaker implant	0.9	0.9	0.8855	0.9	0.9	0.5488	0.8	0.8	0.8797
Stent	2.7	1.9	<0.0001*	2.7	2.1	0.0002*	2.8	2.2	<0.0001*

Table 5.5 Continued

	Depression diagnosis within 30 days after AMI admission		Chi-square test	Depression diagnosis within 60 days after AMI admission		Chi-square test	Depression diagnosis within 90 days after AMI admission		Chi-square test
Variables	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**
Pre-index medication use									
Antidepressants									
SSRIs	8.3	38.8	<0.0001*	7.8	35.2	<0.0001*	7.5	33.4	<0.0001*
SNRIs	1.3	6.2	<0.0001*	1.3	5.6	<0.0001*	1.3	5.2	<0.0001*
TCAs	3.1	6.1	<0.0001*	3.1	5.8	<0.0001*	3.1	5.7	<0.0001*
Other antidepressants	3.2	10.7	<0.0001*	3.0	9.6	<0.0001*	2.9	9.1	<0.0001*
ACE inhibitors	36.2	35.9	0.5509	36.1	36.5	0.4763	36.1	36.3	0.5511
ARBs	18.6	18.1	0.2294	18.7	18.5	0.5145	18.7	18.8	0.8096
β-blcokers	48.4	47.9	0.3882	48.2	48.2	0.9221	48.1	48.3	0.7099
CCBs	30.8	30.8	0.9692	30.7	31.1	0.4300	30.7	31.1	0.3660
Clopidogrel	16.8	16.3	0.1944	16.7	16.9	0.5301	16.6	17.2	0.0806
Diuretics	50.1	50.8	0.1482	49.6	51.1	0.0014*	49.2	51.4	<0.0001*
Nitrates	23.5	22.8	0.0879	23.3	23.3	0.9379	23.1	23.0	0.8626
Statins	42.2	40.7	0.0044*	42.4	41.6	0.1303	42.5	42.0	0.3369
Contextual factors									
Urban living									
Metropolitan	69.3	71.5	<0.0001*	69.2	72.3	<0.0001*	69.1	72.3	<0.0001*
Non-metropolitan	30.6	28.5	<0.0001*	30.8	27.6	<0.0001*	30.9	27.7	<0.0001*
Unknown	0.0	0.0	0.8780	0.0	0.1	0.1298	0.0	0.1	0.5149
Neighborhood problems									
Above median crime rate	54.6	53.4	0.0239*	54.5	53.8	0.0972	54.6	53.8	0.0984
Missing crime rate	29.5	30.9	0.0042*	29.5	31.0	0.0005*	29.4	30.9	0.0002*

Table 5.5 Continued

	Depression diagnosis within 30 days after AMI admission		Chi-square test	Depression diagnosis within 60 days after AMI admission		Chi-square test	Depression diagnosis within 90 days after AMI admission		Chi-square test
Variables	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**
Contextual factors (continued)									
Walkability									
Above median walkability	47.0	47.6	0.2293	46.9	47.7	0.1187	46.9	47.6	0.1115
Missing walkability	0.0	0.1	0.8491	0.0	0.1	0.5525	0.0	0.1	0.8123
Residential mobility									
Above median residence (5+ years)	70.1	70.8	0.1463	70.0	70.9	0.0517	70.0	71.0	0.0250*
Missing residence	0.1	0.1	0.5868	0.1	0.1	0.6813	0.1	0.1	0.9902
Socioeconomic disadvantage									
Above median income	55.8	59.1	<0.0001*	55.7	59.0	<0.0001*	55.8	58.5	<0.0001*
Above median poverty	51.1	47.9	<0.0001*	51.1	48.3	<0.0001*	51.0	48.9	<0.0001*
Above median high school degrees	49.2	53.3	<0.0001*	49.2	52.9	<0.0001*	49.2	52.3	<0.0001*
Missing socioeconomics	0.0	0.0	0.9943	0.0	0.0	0.9809	0.0	0.0	0.7578
Climate									
Above median sunshine	45.5	42.7	<0.0001*	45.7	42.4	<0.0001*	45.8	42.7	<0.0001*
Above median temperature	64.3	60.8	<0.0001*	64.3	61.1	<0.0001*	64.4	61.6	<0.0001*
Above median precipitation	37.0	40.0	<0.0001*	37.0	39.7	<0.0001*	36.9	39.6	<0.0001*

Table 5.5 Continued

	Depression diagnosis within 30 days after AMI admission		Chi-square test	Depression diagnosis within 60 days after AMI admission		Chi-square test	Depression diagnosis within 90 days after AMI admission		Chi-square test
Variables	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**	**No**	**Yes**	**P value**
One-year outcomes									
Survival	79.6	72.9	<0.0001*	83.0	74.6	<0.0001*	85.5	77.4	<0.0001*
Total healthcare cost	26075.1	29239.9	<0.0001*	22379.5	26906.6	<0.0001*	19494.1	24162.9	<0.0001*
Part A	15220.8	18270.6	<0.0001*	12548.1	16470.9	<0.0001*	10655.0	14407.0	<0.0001*
Part B	7754.9	7504.5	0.0336	6932.0	7184.9	0.0108*	6174.5	6708.8	<0.0001*
Outpatient	2506.6	2180.7	<0.0001*	2283.3	2136.9	0.0147*	2045.9	2060.3	0.7675
Physician fee schedule	3513.3	3565.8	0.2520	3073.1	3348.2	<0.0001*	2713.6	3049.2	<0.0001*
Others	1735.0	1758.1	0.6126	1575.5	1699.8	0.0012*	1415.0	1599.2	<0.0001*
Part D	3099.3	3464.8	<0.0001*	2899.4	3250.8	<0.0001*	2664.7	3047.1	<0.0001*
Healthcare utilization									
# of hospitalizations	1.1	1.2	<0.0001*	1.0	1.1	<0.0001*	0.8	1.0	<0.0001*
# of ED visits	1.5	1.6	<0.0001*	1.3	1.5	<0.0001*	1.1	1.4	<0.0001*
# of outpatient visits	7.1	7.0	0.4385	6.3	6.6	0.0008*	5.6	6.1	<0.0001*
# of physician visits	23.3	24.5	<0.0001*	19.5	22.8	<0.0001*	17.2	20.7	<0.0001*
# of prescription claims	54.0	61.8	<0.0001*	50.3	58.4	<0.0001*	46.1	54.8	<0.0001*

Notes:

This table describes patient characteristics for the three analytical samples across depression diagnosis groups;
Chi-square test was used to examine differences in characteristic value across patients grouped by depression diagnosis. For example, the p value for anxiety tests whether the difference in anxiety rates exists across depression diagnosis groups.
*significant at 95% CI;

Table 5.5 Continued

Notes (Continued):

Pre-index medical conditions and therapy/procedures were measured in the previous 12 months before the index AMI admission;
Pre-index medication was measured in the previous 6 months before the index AMI admission;
SSRI (selective serotonin reuptake inhibitor);
SNRI (selective-norepinephrine reuptake inhibitor);
TCA (tricyclic antidepressants);
Other antidepressants included bupropion, traZODONE, maprotiline, isocarboxazid, phenelzine, tranylcypromine, selegiline, nefazodone, mirtazapine, St. John's wort, and 5-hydroxytryptophan.
ACEI (angiotensin-converting enzyme inhibitor);
ARB (angiotensin II receptor blockers);
Statins (HMG-CoA reductase inhibitors);
ED (emergency department);
Analysis of variance (ANOVA) test was used to examine differences in characteristic value across patients diagnosed with depression in varying observation windows for continuous variables, including all healthcare cost and utilization measures;
Means were reported for continuous variables;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Table 5.5 Continued

Notes (Continued):

ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;

Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.

Table 5.6. Risk adjustment estimates of the effectiveness of depression diagnosis among elderly patients with acute myocardial infarction

30-day observation window	**Unadjusted differences in outcomes**	**Estimate**	**Standard error**	**P value**
Survival	-0.07	-0.04**	0.01	<0.01
Total healthcare cost	3164.82	2544.43**	337.98	<0.01
Part A	3049.72	2417.63**	269.98	<0.01
Part B	-250.42	129.85	105.09	0.22
Outpatient	-325.90	168.25**	44.53	<0.01
Physician fee schedule	52.50	17.83	44.64	0.69
Others	23.10	-3.05	36.75	0.93
Part D	365.52	-3.05	36.75	0.93
Healthcare utilization				
# of hospitalizations	0.09	0.08**	0.02	<0.01
# of ED visits	0.17	0.11**	0.02	<0.01
# of outpatient visits	-0.07	-0.06	0.09	0.51
# of physician visits	1.20	1.97**	0.25	<0.01
# of prescription claims	7.71	1.23**	0.46	<0.01
60-day observation window				
Survival	-0.08	-0.06**	0.01	<0.01
Total healthcare cost	4527.05	3532.40**	286.94	<0.01
Part A	3922.79	3160.00**	228.52	<0.01
Part B	252.91	381.08	91.28	<0.01
Outpatient	-146.40	7.12	48.40	0.88
Physician fee schedule	275.10	298.32**	38.56	<0.01
Others	124.30	75.64**	38.13	0.05
Part D	351.36	-8.69	30.40	0.78
Healthcare utilization				
# of hospitalizations	0.17	0.13**	0.02	<0.01
# of ED visits	0.22	0.14**	0.02	<0.01
# of outpatient visits	0.26	-0.60	0.88	0.50
# of physician visits	3.30	2.74**	0.21	<0.01
# of prescription claims	8.05	1.91**	0.38	<0.01

Table 5.6 Continued

90-day observation window	Unadjusted differences in outcomes	Estimate	Standard error	P value
Survival	-0.08	-0.06**	0.01	<0.01
Total healthcare cost	4668.78	3600.02**	251.02	<0.01
Part A	3752.00	2979.33**	199.80	<0.01
Part B	534.32	575.99	81.36	<0.01
Outpatient	14.40	326.33**	34.10	<0.01
Physician fee schedule	335.60	123.66**	33.90	<0.01
Others	184.20	44.70*	26.52	0.09
Part D	382.46	44.70*	26.52	0.09
Healthcare utilization				
# of hospitalizations	0.19	0.14**	0.01	<0.01
# of ED visits	0.25	0.16**	0.02	<0.01
# of outpatient visits	0.51	0.40**	0.07	<0.01
# of physician visits	3.50	2.89**	0.19	<0.01
# of prescription claims	8.69	2.96**	0.33	<0.01

Notes:

Unadjusted differences in outcomes were calculated across depression diagnosis groups. For example, unadjusted differences in total 1-year healthcare cost equal average healthcare cost for patients with a depression diagnosis minus average healthcare cost for patients without a depression diagnosis;
All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, and medication use, and contextual factors;
ED (emergency department);
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Table 5.6 Continued

Notes (Continued):

ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death; Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death; Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death; Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.**significant at 95% CI; *significant at 90% CI.

Table 5.7. Patient characteristics across area diagnosis ratio-based instrument groups among elderly patients with acute myocardial infarction (Medicare claims)

n=155841	Area diagnosis ratio (quintiles, 150-person area size)					Armitage trend test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**P value**
n	31166	31168	31173	31163	31171	
Depression diagnosis	3.2	4.9	5.7	6.7	9	<0.0001*
Demographics						
Age						
66-70	19.4	18.7	18.6	18.1	18	<0.0001*
71-75	19.6	19	19	18.7	18.2	<0.0001*
76-80	20.6	20.3	20	20.4	20.1	0.3337
81-85	18.5	19	19.4	19.6	19.4	0.0007*
85+	21.9	23	23.1	23.2	24.2	<0.0001*
Race						
White	82.4	82.7	82.7	83.1	81.8	0.1894
Black	10.8	9.1	7.9	7.8	7.3	<0.0001*
Hispanic	3.9	5.3	5.9	5.9	7.4	<0.0001*
Asian	1.7	1.9	2.4	1.9	2.3	<0.0001*
American native	0.6	0.5	0.4	0.6	0.4	0.0832
Other race	0.4	0.4	0.5	0.5	0.6	0.0041*
Unknown race	0.2	0.2	0.2	0.2	0.2	0.2091
Female	57.2	57.7	56.7	57	56.9	0.176
Low income subsidy	6.7	6.5	5.8	6.3	6.2	0.0100*

Table 5.7 Continued

n=155841	Area diagnosis ratio (quintiles, 150-person area size)					Armitage trend test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**P value**
Pre-index medical conditions						
Charlson comorbidity scores						
0	34.2	33.5	33.6	33.6	32.9	0.0044*
1	23.4	22.8	23.1	22.7	22.9	0.1241
2	14	14.6	14.4	14.6	14.3	0.4101
3	10.4	10.4	10.5	10.3	10.7	0.2909
4+	18	18.7	18.4	18.8	19.2	0.0004*
Mental illnesses						
Anxiety	6.4	6.5	6.6	6.7	6.6	0.1712
Bipolar disorder	0.7	0.6	0.7	0.7	0.7	0.9133
Schizophrenia	0.6	0.6	0.6	0.6	0.7	0.0423*
Alzheimer	11	11.6	11.3	11.1	11.7	0.1398
Substance use disorder	1.3	1.4	1.4	1.2	1.2	0.1292
Unstable angina	8.9	8.7	8.8	9	9.2	0.0757
Cardiac Arrest	0.4	0.4	0.4	0.4	0.4	0.4474
Ventricular Arrhythmia	3.2	3.1	3.4	3.3	3.6	0.0087*
Other cardiac arrhythmia	31.3	32	32.9	32.8	34.2	<0.0001*
Atrial fibrillation	13	13.6	13.6	13.7	14.6	<0.0001*
Stroke	5.5	5.4	5.3	5.3	5.4	0.2517
Ischemic heart disease	55.3	56	56.2	56.5	57.6	<0.0001*
Heart failure	31.6	32.3	32.4	32.1	32.9	0.0036*
Transient ischemic attack	1.8	1.8	2	1.9	1.8	0.8848

Table 5.7 Continued

n=155841	Area diagnosis ratio (quintiles, 150-person area size)					Armitage trend test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**P value**
Pre-index medical conditions (continued)						
Hyperlipidemia	64.2	65.1	65.4	66.5	67.4	<0.0001*
Hypertension (complicated)	6.2	6.4	6.3	6.2	6.5	0.5089
Hypertension (uncomplicated)	81.2	81.5	81.4	81.5	81.7	0.1756
Chronic kidney disease	19	19.3	19	18.9	19.6	0.2647
Diabetes	38	38.2	37.8	37.9	38.3	0.7036
Chronic obstructive pulmonary disease	25.5	26.1	25.9	25.9	26.5	0.0173*
Asthma	6.6	7.2	7.3	7.1	7.1	0.0300*
Any malignancy	8.7	8.7	9.4	9.2	9.6	<0.0001*
Meta solid tumor	2	2.1	2.1	2.2	2.1	0.2151
Pre-index therapy/procedures						
Psychotherapy	0.5	0.6	0.7	0.7	0.9	<0.0001*
Coronary artery bypass grafting	0.5	0.5	0.5	0.5	0.5	0.7186
Percutaneous coronary intervention	0.8	0.8	0.7	0.8	0.8	0.4415
Pacemaker implant	1	0.9	0.8	0.9	0.9	0.758
Stent	2.7	2.5	2.6	2.9	2.6	0.9478
Pre-index medication use						
Antidepressants						
SSRIs	10	10.4	10	10	9.9	0.2421
SNRIs	1.6	1.6	1.7	1.7	1.5	0.5801
TCAs	3.6	3.5	3.3	3.1	3	<0.0001*
Other antidepressants	3.6	3.9	3.5	3.5	3.6	0.2273

Table 5.7 Continued

n=155841	Area diagnosis ratio (quintiles, 150-person area size)					Armitage trend test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**P value**
Pre-index medication use (Continued)						
ACEIs	37	36.1	35.9	36.4	35.7	0.0078*
ARBs	18.2	18.5	18.7	18.7	18.9	0.0120*
β-blockers	47.3	48	48.4	48.9	49.2	<0.0001*
CCBs	30.7	31.1	30.7	30.2	31.1	0.9241
Clopidogrel	16.8	16.6	16.6	16.6	17.2	0.2934
Diuretics	51	50.9	49.7	49.6	49.3	<0.0001*
Nitrates	23.6	23.2	23.4	23.6	23.7	0.425
Statins	41.3	42	41.7	42.6	42.7	0.0002*
Contextual factors						
Urban living						
Metropolitan	66.6	70.3	68.5	70.1	71.7	<0.0001*
Non-metropolitan	33.3	29.6	31.4	29.8	28.3	<0.0001*
Unknown	0	0.1	0	0.1	0	0.1157
Neighborhood problems						
Above median crime rate	57.8	51.9	50.6	56.4	55.9	0.526
Missing crime rate	26.9	31.3	31.1	29.4	29.3	0.0003*
Walkability						
Above median walkability	43.1	47.8	49.2	47	47.9	<0.0001*
Missing walkability	0.1	0	0.1	0.1	0	0.0546

Table 5.7 Continued

n=155841	Area diagnosis ratio (quintiles, 150-person area size)					Armitage trend test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**P value**
Contextual factors (continued)						
Residential mobility						
Above median residence (5+ years)	72.1	71.1	69.4	67.2	70.7	<0.0001*
Missing residence	0	0	0.1	0.1	0	0.3904
Socioeconomic disadvantage						
Above median income	55.2	55.2	54.6	57.1	57.7	<0.0001*
Above median poverty	53	51.8	51.5	49.2	49.1	<0.0001*
Above median high school degrees	46.9	49.2	48.7	51.2	51.1	<0.0001*
Missing socioeconomics	0	0	0.1	0.1	0	0.3912
Climate						
Above median sunshine	49.1	43.6	44.9	42.5	46.6	<0.0001*
Above median temperature	67.2	63.3	61.5	62.8	65.6	<0.0001*
Above median precipitation	36.2	38.9	36.4	36.6	37.9	0.1656
One-year outcomes						
Survival	79.2	79.5	79.4	79.0	79.0	0.2021
Total healthcare cost	25336.8	26255.8	26371.9	26371.6	26973.1	<0.0001*
Part A	14822.9	15471.8	15441.9	15415.8	15851.9	<0.0001*
Part B	7439.7	7680.4	7774.0	7837.6	7969.0	<0.0001*
Outpatient	2418.9	2543.1	2506.1	2499.8	2468.6	0.1737
Physician fee schedule	3328.4	3422.1	3508.3	3566.6	3756.7	<0.0001*
Others	1692.4	1715.2	1759.6	1771.1	1743.7	0.1228
Part D	3074.1	3103.6	3156.0	3118.3	3152.3	0.0096*

Table 5.7 Continued

n=155841	Area diagnosis ratio (quintiles, 150-person area size)					Armitage trend test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**P value**
One-year outcomes (continued)						
Healthcare utilization						
# of hospitalizations	1.1	1.1	1.1	1.1	1.1	0.0712
# of ED visits	1.5	1.5	1.5	1.5	1.4	0.1957
# of outpatient visits	6.9	7.1	7.2	7.1	6.9	0.0005*
# of physician visits	21.2	22.0	22.5	22.9	23.6	<0.0001*
# of prescription claims	54.9	55.0	54.8	53.7	54.1	<0.0001*

Notes:

Area diagnosis ratio (ADR) of depression diagnosis was adjusted for patient-level characteristics. Patients were grouped using ADR quintiles. Area diagnosis ratios (ADR) measuring local area practice styles were divided into 5 groups. The ADR-based instruments used in the IV models were a series of binary variables indicating each patient residence ZIP code ADR within the quintiles of the distribution of ADRs across patients. Quintile1 represents the lowest ADR group, while Quintile5 represents the highest ADR group.

Cochran-Armitage test was used to examine trend in characteristic value across patients grouped into quintiles based on local area practice style measures of depression diagnosis. For example, the p value for anxiety tests whether a linear trend in anxiety rates exists across the instrument-based groups; *significant at 95% CI;

Pre-index medical conditions and surgical procedures were measured in the previous 12 months before the index AMI admission;

Pre-index medication use was measured in the previous 6 months before the index AMI admission;

SSRI (selective serotonin reuptake inhibitor);

SNRI (selective-norepinephrine reuptake inhibitor);

TCA (tricyclic antidepressants);

Other antidepressants included bupropion, traZODONE, maprotiline, isocarboxazid, phenelzine, tranylcypromine, selegiline, nefazodone, mirtazapine, St. John's wort, and 5-hydroxytryptophan.

Table 5.7 Continued

Notes (Continued):

ACEI (angiotensin-converting enzyme inhibitor), ARB (angiotensin II receptor blockers);
Statins (HMG-CoA reductase inhibitors); ED (emergency department);
Analysis of variance (ANOVA) test was used to examine differences in characteristic value across patients diagnosed with depression in varying observation windows for continuous variables, including all healthcare cost and utilization measures;
Means were reported for continuous variables;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.

Table 5.8. Chow F values for area diagnosis ratio-based instruments in instrumental variables estimation

Area size	Depression diagnosis within 30 days after AMI admission	Depression diagnosis within 60 days after AMI admission	Depression diagnosis within 90 days after AMI admission
50	765.18	718.53	677.33
60	661.17	626.94	602.87
70	570.92	542.62	522.47
80	503.10	477.77	464.05
90	445.88	427.75	420.12
100	406.68	384.94	390.58
110	369.24	358.00	364.93
120	347.24	326.04	332.13
130	313.68	311.21	322.57
140	296.55	301.16	300.53
150	285.95	288.45	284.59
160	274.99	275.73	267.27
170	260.40	258.57	257.45
180	252.94	250.75	256.16
190	244.25	245.00	249.16
200	235.43	235.09	233.11

Notes:

Chow F-tests examined whether the instruments described a statistically significant portion of variation in depression diagnosis. A “rule of thumb” for a strong instrument relationship is a Chow F-value > 10.[213]

Table 5.9. Instrumental variables estimates of the effectiveness of depression diagnosis among elderly patients with acute myocardial infarction (Area diagnosis ratios)

30-day observation window	Unadjusted differences in outcomes	Estimate	Standard error	P value	Hansen test (P value)
Survival	-0.03	<0.01	0.05	0.96	0.11
Total healthcare cost	28213.47	20723.66**	3805.74	<0.01	0.14
Part A	17740.71	12463.60**	2979.91	<0.01	0.29
Part B	9125.51	7452.22**	1300.81	<0.01	0.11
Outpatient	856.90	726.39	747.97	0.33	0.06
Physician fee schedule	7384.48	5887.32**	557.56	<0.01	0.36
Others	884.48	838.52*	512.71	0.10	0.04
Part D	1347.26	807.83**	398.26	0.04	0.23
Healthcare utilization					
# of hospitalizations	0.58	0.26	0.20	0.19	0.67
# of ED visits	-0.37	-0.50**	0.26	0.05	0.36
# of outpatient visits	-0.47	-0.36	1.07	0.74	0.23
# of physician visits	41.38	32.01**	2.84	<0.01	0.18
# of prescription claims	-13.42	-12.08**	4.53	<0.01	0.04**

Table 5.9 Continued

60-day observation window	Unadjusted differences in outcomes	Estimate	Standard error	P value	Hansen test (P value)
Survival	-0.12	-0.07*	0.04	0.09	0.84
Total healthcare cost	22540.40	22166.13**	3085.1	<0.01	0.67
Part A	14193.73	13764.32**	2378.25	<0.01	0.53
Part B	7808.30	7898.55**	1137.78	<0.01	0.92
Outpatient	490.66	1362.43**	697.65	0.05	0.92
Physician fee schedule	5828.81	4910.71**	449.24	<0.01	0.49
Others	1488.83	1625.41**	457.65	<0.01	0.51
Part D	538.37	503.26	326.9	0.12	0.06*
Healthcare utilization					
# of hospitalizations	0.41	0.37**	0.17	0.02	<0.01**
# of ED visits	-0.64	-0.34*	0.21	0.10	0.02**
# of outpatient visits	-2.01	-0.6	0.88	0.49	<0.01**
# of physician visits	34.93	27.13**	2.22	<0.01	1.00
# of prescription claims	-16.05	-12.61**	3.65	<0.01	0.45

Table 5.9 Continued

90-day observation window	Unadjusted differences in outcomes	Estimate	Standard error	P value	Hansen test (P value)
Survival	-0.08	-0.03	0.04	0.39	0.70
Total healthcare cost	17456.64	21366.37**	2664.35	<0.01	0.95
Part A	10502.96	13794.72**	2054.71	<0.01	1.00
Part B	5981.37	6850.00**	986.31	<0.01	0.66
Outpatient	541.04	1287.62**	612.14	0.04	0.35
Physician fee schedule	4761.83	3923.13**	386.15	<0.01	0.52
Others	678.50	1639.25**	394.42	<0.01	0.45
Part D	972.31	721.66**	285.8	0.01	0.41
Healthcare utilization					
# of hospitalizations	0.39	0.33**	0.14	0.02	0.69
# of ED visits	-0.29	-0.2	0.19	0.29	0.99
# of outpatient visits	-0.03	0.99	0.76	0.19	<0.01**
# of physician visits	25.00	21.64**	1.88	<0.01	0.24
# of prescription claims	-8.27	-8.3**	3.12	<0.01	0.19

Notes:

Unadjusted differences in 1-year outcomes were calculated across the 1st and 5th ADR quintile groups. For example, unadjusted differences in total 1-year healthcare cost equal average healthcare cost for patients in the 5th ADR quintile group minus average healthcare cost for patients in the 1st ADR quintile group;
All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
ED (emergency department);

Table 5.9 Continued

Notes(Continued):

Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;

Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;

Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;

Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;

Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.

**significant at 95% CI; *significant at 90% CI;

Hansen over-identification tests were used to examine whether excluding the area diagnosis ratio (ADR)-based instruments from the second stage of 2SLS was appropriate (null hypothesis)[214]

Table 5.10. Patient characteristics across individual physician practice style-based instrument groups among elderly patients with acute myocardial infarction (Medicare claims)

	Individual physician diagnosis rate (prior 6 months)		Chi-square test	
Variables	**0**	**>0**	**P value**	**Total (%)**
n	142888	12843		155371
Depression diagnosis	5.5	10.9	<0.0001*	9192(5.9%)
Demographics				
Age				
66-70	18.7	16.8	<0.0001*	28910(18.6%)
71-75	19	17.2	<0.0001*	29416(18.9%)
76-80	20.3	20.4	0.7047	31581(20.3%)
81-85	19.1	20.5	<0.0001*	29875(19.2%)
85+	22.9	25.1	<0.0001*	35949(23.1%)
Race				
White	82.4	84.1	<0.0001*	128570(82.6%)
Black	8.6	8.2	0.1423	13333(8.6%)
Hispanic	5.7	5.4	0.1065	8834(5.7%)
Asian	2.1	1.2	<0.0001*	3170(2%)
American native	0.5	0.4	0.3819	772(0.5%)
Other race	0.5	0.4	0.5393	747(0.5%)
Unknown race	0.2	0.2	0.9746	305(0.2%)
Female	56.9	59.8	<0.0001*	88937(57.1%)
Low income subsidy	6.3	6.1	0.2486	9815(6.3%)
Pre-index medical conditions				
Charlson comorbidity scores				
0	33.9	29.8	<0.0001*	52254(33.6%)
1	23	22.7	0.3944	35794(23%)
2	14.3	14.8	0.1928	22377(14.4%)
3	10.4	11.5	0.0001*	16295(10.5%)
4+	18.4	21.3	<0.0001*	29011(18.6%)
Mental illnesses				
Anxiety	6.5	8.2	<0.0001*	10277(6.6%)
Bipolar disorder	0.6	1	<0.0001*	1048(0.7%)
Schizophrenia	0.6	0.9	<0.0001*	942(0.6%)
Alzheimer	11	14.8	<0.0001*	17659(11.3%)
Substance use disorder	1.3	1.6	0.0051*	2031(1.3%)

Table 5.10 Continued

	Individual physician diagnosis rate (prior 6 months)		Chi-square test	
Variables	**0**	**>0**	**P value**	**Total (%)**
Pre-index medical conditions (continued)				
Unstable angina	8.9	8.7	0.3374	13880(8.9%)
Cardiac Arrest	0.4	0.4	0.6765	632(0.4%)
Ventricular Arrhythmia	3.3	3.6	0.0856	5184(3.3%)
Other cardiac arrhythmia	32.4	34.8	<0.0001*	50806(32.6%)
Atrial fibrillation	13.5	15.6	<0.0001*	21319(13.7%)
Stroke	5.2	6.9	<0.0001*	8368(5.4%)
Ischemic heart disease	56.3	56.8	0.3144	87740(56.3%)
Heart failure	32	35.6	<0.0001*	50230(32.3%)
Transient ischemic attack	1.8	2.1	0.0107*	2882(1.9%)
Hyperlipidemia	65.7	65.8	0.8002	102353(65.7%)
Hypertension (complicated)	6.3	7	0.0011*	9834(6.3%)
Hypertension (uncomplicated)	81.3	83.6	<0.0001*	126848(81.5%)
Chronic kidney disease	19	21	<0.0001*	29833(19.2%)
Diabetes	37.8	40.3	<0.0001*	59198(38%)
Chronic obstructive pulmonary disease	25.7	29	<0.0001*	40454(26%)
Asthma	7.1	7.2	0.4202	11017(7.1%)
Any malignancy	9.1	9.9	0.0018*	14206(9.1%)
Meta solid tumor	2.1	2	0.4675	3315(2.1%)
Pre-index therapy/procedures				
Psychotherapy	0.5	0.6	0.0319*	761(0.5%)
Coronary artery bypass grafting	0.8	0.8	0.6383	1231(0.8%)
Percutaneous coronary intervention	0.9	0.9	0.4731	1367(0.9%)
Pacemaker implant	2.7	2.1	0.0001*	4120(2.6%)
Stent	0.7	0.9	0.0006*	1081(0.7%)
Pre-index medication use				
Antidepressants				
SSRIs	9.9	12.4	<0.0001*	15677(10.1%)
SNRIs	1.6	2.1	<0.0001*	2537(1.6%)
TCAs	3.3	3.3	0.7787	5159(3.3%)
Other antidepressants	3.5	4.6	<0.0001*	5662(3.6%)

Table 5.10 Continued

	Individual physician diagnosis rate (prior 6 months)		Chi-square test	
Variables	**0**	**>0**	**P value**	**Total (%)**
ACEIs	36.2	36.7	0.2746	56421(36.2%)
ARBs	18.6	18.9	0.4648	28982(18.6%)
β-blockers	48.2	49.8	0.0007*	75286(48.3%)
CCBs	30.7	31.1	0.3981	47929(30.8%)
Clopidogrel	16.8	17	0.4375	26125(16.8%)
Diuretics	49.9	52.5	<0.0001*	78050(50.1%)
Nitrates	23.4	24.2	0.0477*	36582(23.5%)
Statins	42.1	41.9	0.6164	65550(42.1%)
Contextual factors				
Urban living				
Metropolitan	69.7	67.2	<0.0001*	108163(69.5%)
Non-metropolitan	30.3	32.8	<0.0001*	47495(30.5%)
Unknown	0	0	0.9931	73(0%)
Neighborhood problems				
Above median crime rate	54.6	53.5	0.0130*	84883(54.5%)
Missing crime rate	29.6	29.6	0.9303	46094(29.6%)
Walkability				
Above median walkability	47.1	46.2	0.0546	73229(47%)
Missing walkability	0.1	0	0.5553	78(0.1%)
Residential mobility				
Above median residence (5+ years)	70.2	68.6	0.0001*	109167(70.1%)
Missing residence	0.1	0	0.0558	82(0.1%)
Socioeconomic disadvantage				
Above median income	56.2	53.9	<0.0001*	87185(56%)
Above median poverty	50.8	52	0.0087*	79285(50.9%)
Above median high school degrees	49.6	47.8	0.0002*	76957(49.4%)
Missing socioeconomics	0	0	0.0134*	68(0%)
Climate				
Above median sunshine	45.8	40.6	<0.0001*	70626(45.4%)
Above median temperature	64.4	60.4	<0.0001*	99813(64.1%)
Above median precipitation	36.3	47.5	<0.0001*	57978(37.2%)

Table 5.10 Continued

	Individual physician diagnosis rate (prior 6 months)		Chi-square test	
Variables	**0**	**>0**	**P value**	**Total (%)**
One-year outcomes				
Survival	79.6	75.0	<0.0001*	123370(79.2%)
Total healthcare cost	25997.6	29244.9	<0.0001*	26265.4
Part A	15177.4	17907.1	<0.0001*	15402.6
Part B	7700.7	8196.0	<0.0001*	7741.6
Outpatient	2477.2	2607.6	0.0297*	2488.0
Physician fee schedule	3496.9	3741.9	<0.0001*	3517.1
Others	1726.6	1846.5	0.0021*	1736.5
Part D	3119.5	3141.9	0.4635	3121.3
Healthcare utilization				
# of hospitalizations	1.1	1.3	<0.0001*	1.1
# of ED visits	1.4	1.7	<0.0001*	1.5
# of outpatient visits	7.0	7.5	<0.0001*	7.0
# of physician visits	22.2	24.6	<0.0001*	22.4
# of prescription claims	54.4	56.0	<0.0001*	54.5

Notes:

Individual practice style of depression diagnosis was measured based on depression diagnosis rates for physicians seen by the AMI patients during the first 30 days after the index AMI admission. Only depression diagnosis prior 6 months of the index AMI admission were counted for each individual physician's practice style. Patients were grouped based on whether or not they saw a physician who diagnosed depression prior 6 months of the index AMI admission;
Chi-square test was used to examine differences in characteristic value across patients grouped by depression diagnosis. For example, the p value for anxiety tests whether the difference in anxiety rates exists across depression diagnosis groups. *significant at 95% CI;
Pre-index medical conditions and thereapy/procedures at baseline were measured in the previous 12 months before the index AMI admission;
Pre-index medication use was measured in the previous 6 months before the index AMI admission;
SSRI (selective serotonin reuptake inhibitor);
SNRI (selective-norepinephrine reuptake inhibitor);
TCA (tricyclic antidepressants);
Other antidepressants included bupropion, traZODONE, maprotiline, isocarboxazid, phenelzine, tranylcypromine, selegiline, nefazodone, mirtazapine, St. John's wort, and 5-hydroxytryptophan.

Table 5.10 Continued

Notes (Continued):

ACEI (angiotensin-converting enzyme inhibitor);
ARB (angiotensin II receptor blockers);
Statins (HMG-CoA reductase inhibitors);
ED (emergency department);
Analysis of variance (ANOVA) test was used to examine differences in characteristic value across patients grouped by individual physician practice styles of depression diagnosis for continuous variables, including all healthcare cost and utilization measures;
Means were reported for continuous variables;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.

Table 5.11. Chow F values for physician prior depression diagnosis rates-based instruments in instrumental variables estimation

	Depression diagnosis within 30 days after AMI admission	Depression diagnosis within 60 days after AMI admission	Depression diagnosis within 90 days after AMI admission
Physician prior depression diagnosis rates	305.44	406.25	526.49

Notes:

Chow F-tests examined whether the instruments described a statistically significant portion of variation in depression diagnosis. A "rule of thumb" for a strong instrument relationship is a Chow F-value > 10.[213]

Table 5.12. Instrumental variables estimates of the effectiveness of depression diagnosis among elderly patients with acute myocardial infarction (Physician prior depression diagnosis rates)

30-day observation window	**Unadjusted differences in outcomes**	**Estimate**	**Standard error**	**P-value**
Survival	-0.85	-0.53**	0.08	<0.01
Total healthcare cost	60134.67	47860.73**	6463.75	<0.01
Part A	50548.39	40343.45**	5158.15	<0.01
Part B	9171.71	8342.18**	1977.51	<0.01
Outpatient	2414.81	2245.50**	1103.45	0.04
Physician fee schedule	4537.04	4906.52**	841.82	<0.01
Others	2220.37	1190.17	742.31	0.11
Part D	414.58	-824.91	618.57	0.18
Healthcare utilization				
# of hospitalizations	2.46	1.62**	0.33	<0.01
# of ED visits	3.73	2.57**	0.44	<0.01
# of outpatient visits	8.22	3.90**	1.72	0.02
# of physician visits	43.70	39.03**	4.80	<0.01
# of prescription claims	29.39	2.15	7.17	0.77
60-day observation window				
Survival	-0.84	-0.60**	0.07	<0.01
Total healthcare cost	61595.28	48564.88**	4899.36	<0.01
Part A	48981.19	39605.86**	3885.18	<0.01
Part B	11270.81	9122.22*	1526.58	<0.01
Outpatient	2868.10	2090.26**	846.53	0.01
Physician fee schedule	5334.98	4892.50**	626.75	<0.01
Others	3249.72	2139.46**	615.93	<0.01
Part D	1343.29	-163.20	473.02	0.73
Healthcare utilization				
# of hospitalizations	2.75	1.93**	0.26	<0.01
# of ED visits	3.87	2.83**	0.35	<0.01
# of outpatient visits	7.41	4.24**	1.28	<0.01
# of physician visits	47.58	41.19**	3.68	<0.01
# of prescription claims	40.84	12.70*	5.33	0.02

Table 5.12 Continued

90-day observation window				
Survival	-0.72	-0.52**	0.05	<0.01
Total healthcare cost	57527.73	45115.47**	3895.77	<0.01
Part A	42526.42	33805.01**	3028.38	<0.01
Part B	13384.35	11233.65**	1271.75	<0.01
Outpatient	3909.54	3369.31**	678.28	<0.01
Physician fee schedule	5532.38	4843.11**	511.18	<0.01
Others	3942.44	3021.24**	526.84	<0.01
Part D	1616.96	76.81	354.74	0.83
Healthcare utilization				
# of hospitalizations	2.46	1.68**	0.20	<0.01
# of ED visits	3.34	2.37**	0.26	<0.01
# of outpatient visits	8.09	5.73**	1.01	<0.01
# of physician visits	88.12	37.62**	2.87	<0.01
# of prescription claims	44.49	23.23**	4.20	<0.01

Notes:

Unadjusted differences in outcomes were calculated across prior physician depression diagnosis groups. For example, unadjusted differences in total 1-year healthcare cost equal average healthcare cost for patients seeing physicians who gave a depression diagnosis in the previous 6 months before the index AMI admission date minus average healthcare cost for patients seeing physician who did not give a depression diagnosis in the period;

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, and medication use, and contextual factors;

ED (emergency department);

Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;

Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;

Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;

Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;

Table 5.12 Continued

Notes (Continued):

ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.
**significant at 95% CI; *significant at 90% CI

Table 5.13. Patient characteristics across depression diagnosis groups among elderly patients with acute myocardial infarction (hospital charts)

	Depression diagnosis		**Chi-square test**	**N=1403**
Variables	**No**	**Yes**	**p value**	**Total (%)**
n	**1331**	**72**		
Depression diagnosis	0	100	<0.0001*	72(5.1%)
Difficulty with activities of daily living				
Dressing/undressing	2.5	1.4	0.5578	34(2.4%)
Feeding oneself	1.6	0	0.2829	21(1.5%)
Functional transfers	4.4	4.2	0.9383	61(4.3%)
Incontinence/elimination difficulties	3.9	1.4	0.2751	53(3.8%)
Personal hygiene/grooming	2.9	2.8	0.9404	41(2.9%)
Cane user	10.7	11.1	0.922	151(10.8%)
Walker user	13.7	16.7	0.4858	195(13.9%)
Wheelchair user	5.2	5.6	0.8901	73(5.2%)
Other limited range of motion/in physical therapy	0.5	0	0.5373	7(0.5%)
Activities of daily living unspecified	2.8	5.6	0.1732	41(2.9%)
Bed bound	0.8	0	0.4387	11(0.8%)
Adult comorbidity evaluation-27				
None	4.7	2.8	0.442	65(4.6%)
Mild	36.1	36.1	0.9934	506(36.1%)
Moderate	22.4	31.9	0.0601	321(22.9%)
Severe	36.8	29.2	0.189	511(36.4%)
AMI severity score	9.8	10.4	0.3585	9.9
Mental illnesses				
Depression or bipolar disorder	0.5	5.6	<0.0001*	10(0.7%)
Dementia	10.6	18.1	0.0485*	162(11%)
Alcohol abuse	2.7	2.8	0.9703	46(2.7%)
Other mental illnesses	0.5	5.6	<0.0001*	11(0.8%)

Notes:

AMI: acute myocardial infarction;
Chi-square test was used to examine differences in characteristic value across patients grouped by depression diagnosis. *significant at 95% CI;
Difficulty with activities[217], adult comorbidity evaluation-27[216], AMI severity score based on expert opinion, and mental illnesses were extracted from hospital charts during the index hospitalization for acute myocardial infarction;

Table 5.13 continued.

Notes:

Analysis of variance (ANOVA) test was used to examine differences in characteristic value across depression diagnosis groups for continuous variable of AMI severity score;

Means were reported for continuous variables;

.

Table 5.14. Patient characteristics across area diagnosis ratios instrument groups among elderly patients with acute myocardial infarction (hospital charts)

	Area diagnosis ratios instrument groups					Armitage test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**p value**
n	**282**	**283**	**273**	**295**	**270**	
Depression diagnosis	3.2	3.9	5.1	6.4	7	0.0140*
Difficulty with activities of daily living						
Dressing/undressing	1.8	2.5	3.7	1.7	2.6	0.7778
Feeding oneself	1.1	1.4	2.2	1	1.9	0.6198
Functional transfers	2.8	2.8	4	7.1	4.8	0.0289*
Incontinence/elimination difficulties	2.8	3.2	4	4.1	4.8	0.1813
Personal hygiene/grooming	2.8	3.2	2.2	3.1	3.3	0.7915
Cane user	10.3	12	11.4	10.2	10	0.6817
Walker user	11	14.8	12.8	15.3	15.6	0.1441
Wheelchair user	4.6	3.5	5.1	5.8	7	0.0941
Other limited range of motion/in physical therapy	0.7	0.4	0.4	0.3	0.7	0.9872
Activities of daily living unspecified	4.6	3.2	1.5	2	3.3	0.231
Bed bound	0	1.1	0.7	0.7	1.5	0.1275
AMI severity score	9.8	9.8	10.0	10.1	9.6	0.7992
Adult comorbidity evaluation-27						
None	4.3	5.7	4.8	3.1	5.6	0.9681
Mild	33.7	31.1	38.1	41.4	35.9	0.0949
Moderate	27	25.4	20.5	22	19.3	0.0184*
Severe	35.1	37.8	36.6	33.6	39.3	0.683

Table 5.14 Continued

	Area diagnosis ratios instrument groups					Armitage test
Variables	**Quintile1**	**Quintile2**	**Quintile3**	**Quintile4**	**Quintile5**	**p value**
Mental illnesses						
Depression or bipolar disorder	1.1	0.4	0	0.3	1.9	0.3575
Dementia	10.3	12.7	9.5	9.2	13.3	0.7018
Alcohol abuse	1.8	3.9	3.3	2.4	2.2	0.845
Other mental illnesses	0.4	1.1	1.5	0.3	0.7	0.9839

Notes:

AMI: acute myocardial infarction;
Patients were grouped using quintile groups of area diagnosis ratio (ADR).
Cochran-Armitage test was used to examine trend in characteristic value across patients grouped into quintiles based on local area practice style measures of depression diagnosis. *significant at 95% CI;
Difficulty with activities[217], adult comorbidity evaluation-27[216], AMI severity score based on expert opinions and mental illnesses were extracted from hospital charts during the index hospitalization for acute myocardial infarction;
Analysis of variance (ANOVA) test was used to examine differences in characteristic value across patients grouped by local area depression diagnosis styles for continuous variable of AMI severity score;
Means were reported for continuous variables;

Table 5.15. Patient characteristics across individual physician practice styles-based instrument groups among elderly patients with acute myocardial infarction (hospital charts)

	Individual physician diagnosis rates (prior 6 months)		**Chi-square test**	**N=1401**
Variables	**0**	**>0**	**p value**	**Total (%)**
n	**1289**	**112**		
Depression diagnosis	5	6.3	0.5788	72(5.1%)
Difficulty with activities of daily living				
Dressing/undressing	2.4	2.7	0.8568	34(2.4%)
Feeding oneself	1.6	0.9	0.5821	21(1.5%)
Functional transfers	4.5	2.7	0.365	61(4.4%)
Incontinence/elimination difficulties	3.9	2.7	0.523	53(3.8%)
Personal hygiene/grooming	2.8	4.5	0.3141	41(2.9%)
Cane user	10.5	14.3	0.212	151(10.8%)
Walker user	13.7	17	0.3316	195(13.9%)
Wheelchair user	5.1	6.3	0.6058	73(5.2%)
Other limited range of motion/in physical therapy	0.5	0.9	0.5384	7(0.5%)
Activities of daily living unspecified	2.9	3.6	0.6729	41(2.9%)
Bed bound	0.7	1.8	0.211	11(0.8%)
Adult comorbidity evaluation-27				
None	4.4	7.1	0.1892	65(4.6%)
Mild	36.9	26.8	0.0333*	505(36%)
Moderate	22.5	27.7	0.2108	321(22.9%)
Severe	36.2	38.4	0.6481	510(36.4%)
AMI severity score	9.9	9.8	0.9600	9.9
Mental illnesses				
Depression or bipolar disorder	0.8	0	0.3495	10(0.7%)
Dementia	10.6	15.2	0.1398	154(11%)
Alcohol abuse	2.9	0	0.0654	38(2.7%)
Other mental illnesses	0.9	0	0.3263	11(0.8%)

Notes:

AMI: acute myocardial infarction;

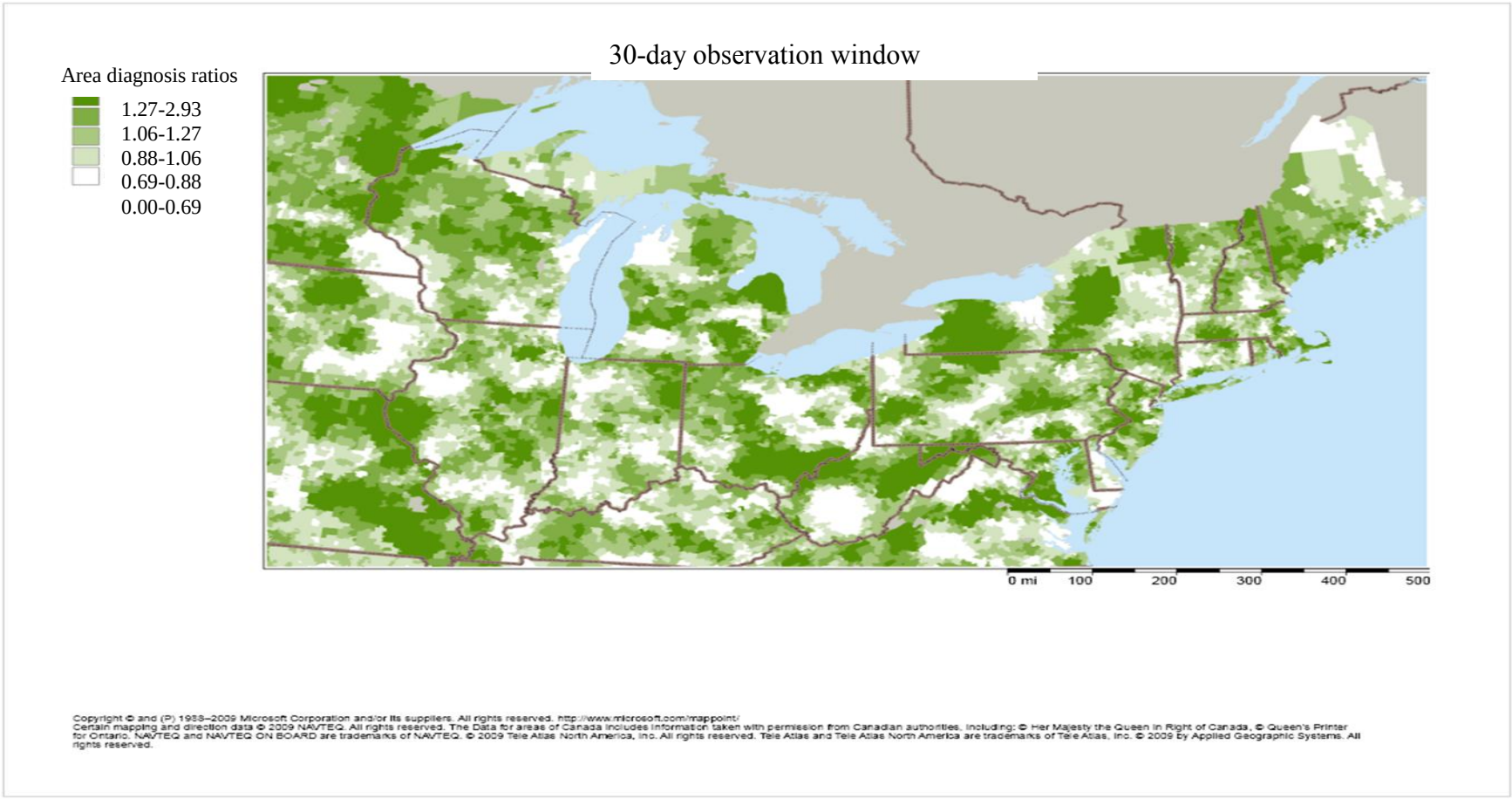
Chi-square test was used to examine differences in characteristic value across patients grouped by physician prior depression diagnosis rates. *significant at 95% CI;

Table 5.15 Continued

Notes:

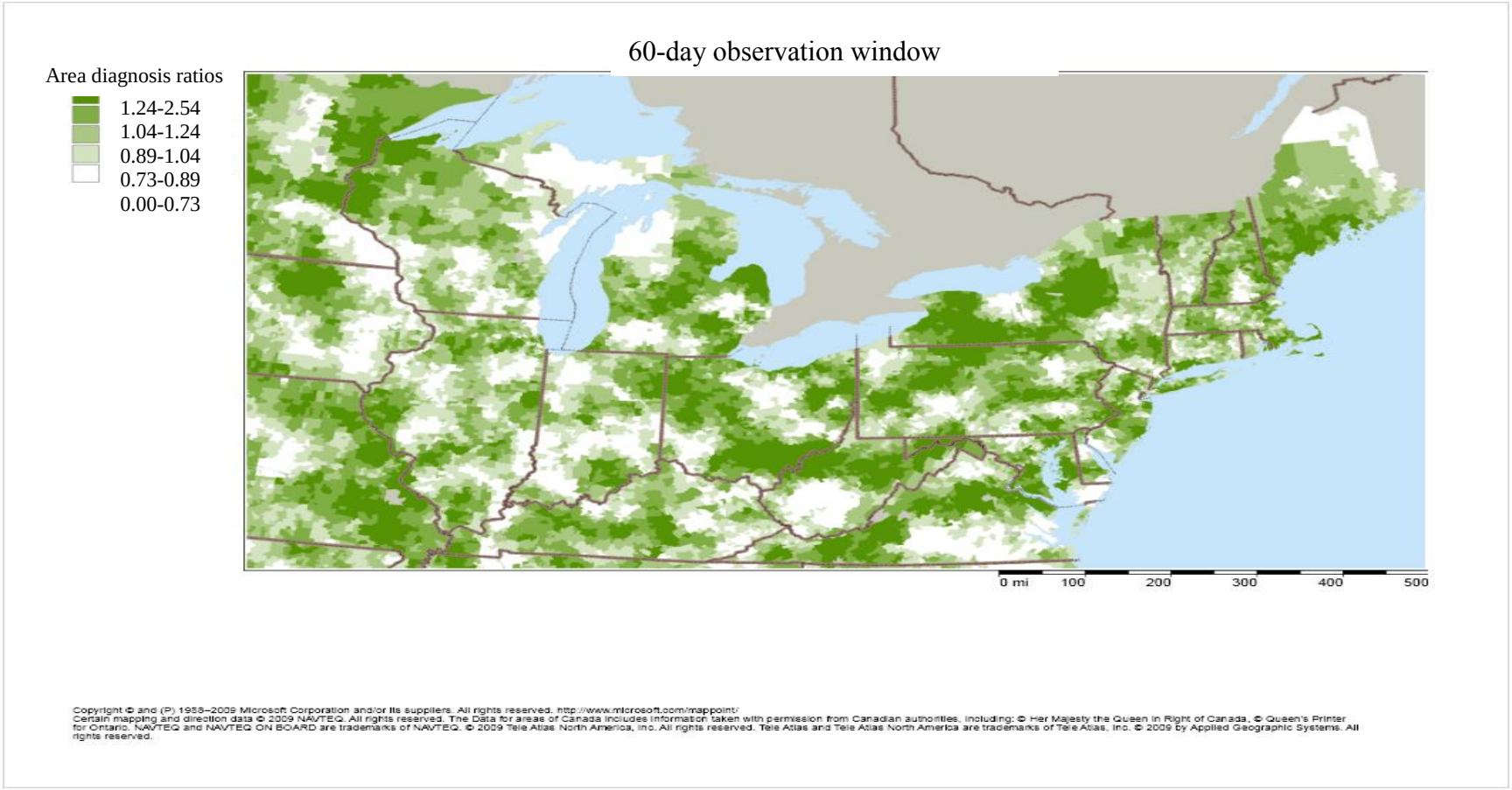
Difficulty with activities[217], adult comorbidity evaluation-27[216], AMI severity score based on expert opinions and mental illnesses were extracted from hospital charts during the index hospitalization for acute myocardial infarction. Analysis of variance (ANOVA) test was used to examine differences in characteristic value across patients grouped by individual physician practice styles of depression diagnosis for continuous variable of AMI severity score; Means were reported for continuous variables;

Figure 5.1. Northeastern United States depression area diagnosis ratios (ADRs)-based on local areas defined by 150 patients around each ZIP code



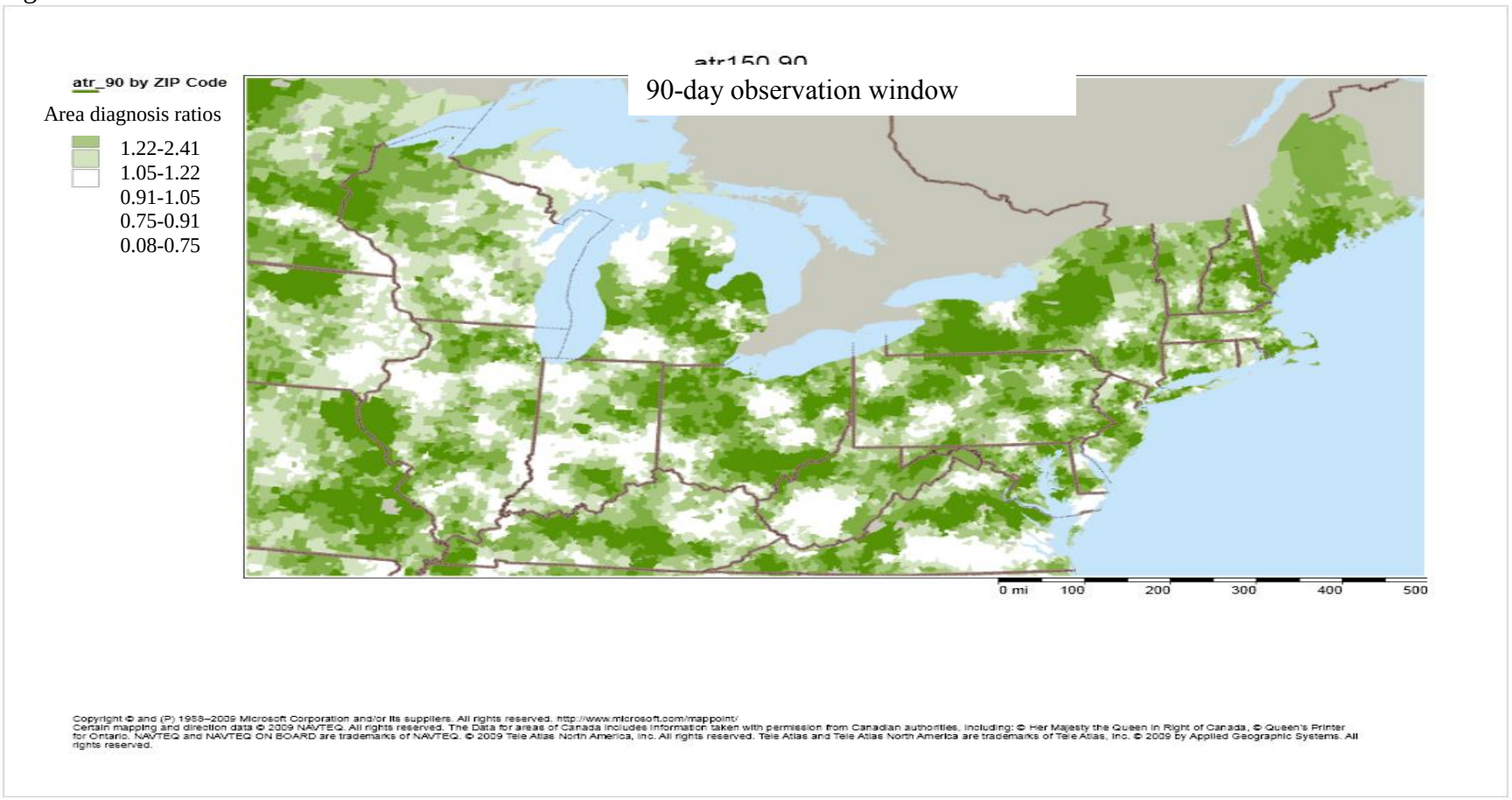
a. Depression diagnosis within 30 days after acute myocardial infarction

Figure 5.1. Continued



b. Depression diagnosis within 60 days after acute myocardial infarction

Figure 5.1. Continued



c. Depression diagnosis within 90 days after acute myocardial infarction

CHAPTER VI

DISCUSSION

Main findings

Using observational data, this dissertation evaluated whether the existing diagnosis rates were "right" using both RA and IV estimators with correct interpretations. More importantly, we proposed a systematic analytical approach to assess the "right" rate question using AMI patients as an example. Given the linkage of depression to worsening cardiovascular outcomes[103-106] and the variation in depression diagnosis rates across studies[53, 128, 129], understanding how depression diagnosis affects outcomes in elderly patients with acute medical conditions is important. In general, RA estimators revealed that depression diagnosis was associated with significant survival loss and increased healthcare costs and utilization in 1 year for patients diagnosed with depression. In IV analysis, higher depression diagnosis rates were only related to increased healthcare costs and physician visits, but lower ED visits and prescription claims for the marginal patients whose depression diagnosis was affected by the ADR-based instruments. The differences in these findings might be explained by distinctions in applications of the estimates from the different analytical approaches across study populations and the validity of assumptions underlying each estimator. Understanding these differences is critical to interpreting our study results and answering the "right" diagnosis rate question.

Interpretation of RA estimates

RA estimators yield estimates of average treatment effects for patients who received a treatment and rely on the assumption that unmeasured factors affecting outcomes are not related to the treatment in study. In this dissertation, with treatment being depression diagnosis, our RA estimates should be interpreted as the average effects of depression diagnosis for AMI patients who received a depression diagnosis and address the specific question of whether, on average, the diagnosis led to benefits to the diagnosed patients. Across the 3 analytical samples with 30, 60, and 90 day observation

windows, depression diagnosis was consistently associated with decreased survival, increased healthcare costs (total and Part A) and healthcare utilization (hospitalizations, ED visits, physician visits, and prescription claims) in 1 year for patients diagnosed with depression.

First, both unadjusted and RA estimates of depression diagnosis on outcomes were larger as observation windows increased from 30 to 90 days. For example, a depression diagnosis within 30 days after the index AMI admission was associated with, on average, $2544 increase in 1-year total healthcare costs, compared with over $3500 increase associated with a diagnosis in 60 days after admission. The increased healthcare costs might be explained by differences in patient characteristics across the diagnosis groups in varying observation windows. As shown in Table 5.4, patients diagnosed with depression within 30 days after the index AMI admission were more likely to be younger and have fewer pre-index comorbidities than those diagnosed in the later periods. Furthermore, patients diagnosed earlier tended to have relatively lower healthcare costs and utilization. Therefore, the observed higher healthcare costs associated with depression diagnosis within 60/90 days after AMI admission might be explained by these patients being sicker than those diagnosed within the first 30 days after AMI admission. It is also possible that patients diagnosed earlier received earlier depression treatment that quickly delayed disease progression than those diagnosed in the later periods.[221] Early detection with appropriate depression treatment maybe helped prevent relapses and reduce healthcare costs and utilization in future. Late depression diagnosis and treatment might still be effective, but outcome changes might take longer to develop in those patients compared with those who were diagnosed earlier.

Second, our RA estimates of the effects of depression diagnosis might be biased toward lower survival and higher healthcare costs and utilization than the true effects. As shown in Table 5.5 using Medicare claims data, compared with undiagnosed patients with depression after AMI admission, the diagnosed patients were more likely to be

older, have some comorbidities such as stroke and hypertension and other mental illnesses prior to AMI admission, and reside in areas with less sunshine, lower temperature, and higher precipitation. Similar patterns might be found for some factors, including a patient's overall health and physical function statuses that were not measured in claims data, but were theorized to affect both depression diagnosis decisions and patient health outcomes. Therefore, we used hospital chart abstracted data to attempt to measure these unmeasured confounders for a subset of patients in our study sample.

Using the chart abstracted data, physical function statuses were measured as difficulties with activities of daily living (ADL)[217] and patient overall health was measured as adult comorbidity evaluation (ACE)-27 (a comprehensive comorbidity index score using disease severity and lab results information) [216], AMI severity, and mental illnesses in charts. Even though the differences in ADL measures were not statistically significant, we observed a higher proportion of patients diagnosed with depression using a cane, walker or wheelchair or other unspecified difficulties with ADL than the undiagnosed. In addition, the diagnosed patients tended to have dementia and other mental illnesses mentioned in charts and have moderate, but not severe comorbidities measured by ACE-27. Therefore, patients diagnosed with depression were more likely to be sicker in unmeasured ways. In this case, the true effects of depression diagnosis might be higher on survival, but lower on healthcare costs and utilization than our RA estimates.

Interpretation of IV estimates

Area diagnosis ratios as instruments

IV estimators yield estimates of the average treatment effects for patients whose treatment choices are affected by the instrument. It has been argued that instrument influenced individuals who are marginal patients whose treatment decisions respond to outside factors, such as policy changes and "cultures" of treatment that affect treatment rates at the population level.[212, 222] IV estimators require the availability of instruments

being strongly related to treatment, with the assumption that the instruments have no direct relationships with outcomes or other unmeasured confounders.[93, 212, 222] Under this assumption, instruments serve as a natural experiment in treatment choice for exploring causal treatment effectiveness using observational data.[85, 212]

In our study, we theorized that our main instrument, local area depression diagnosis styles as measured by area depression diagnosis ratios (ADRs), is unrelated to outcomes such as survival, healthcare costs and utilization of individual patients or unmeasured confounders that affect both outcomes and depression diagnosis, such as patient overall health, physical function statuses, and underlying depression severity. In RCTs, patients are randomly assigned into treatment or control groups, which allows for equal distribution of measured and unmeasured confounders in assigned groups. RCTs therefore are the gold standard in making causal inferences. In our IV analysis, patients were divided into groups based on instrument values associated with the probability of receiving a depression diagnosis after AMI in their local area. This selection process by instrument values that is unrelated to unmeasured confounders serves as a natural experiment in which patients were randomly assigned into groups with different probabilities of receiving a depression diagnosis. For example, patients in the lowest ADR quintile group had a 3.9% probability to be diagnosed with depression within 30 days after depression diagnosis, compared with a 9% chance in the highest ADR quintile group.

Our IV estimates suggested that higher depression diagnosis rates were associated with substantially higher patient healthcare costs and physician visits, but decreased ED visits and prescription claims, for all observational windows (30, 60, and 90 days) post AMI admission. For instance, the estimate of depression diagnosis within 30 days after the index AMI admission on healthcare costs could be interpreted as an additional depression diagnosis associated with an average increase of $20,724 of 1-year total healthcare cost for the marginal patients. In other words, a 1 percentage point increase in

depression diagnosis rate (e.g. from 4% to 5%) for the entire study sample was associated with, on average, a $207.24 increase in the total healthcare costs for an AMI patient. The estimate of depression diagnosis within 30 days after the index AMI admission would have led to an average decrease in 1-year ED visit (0.5) for the marginal patients. Thus, a 1 percentage point increase in depression diagnosis rate for the entire study sample was associated with an average of a 0.005 decrease in ED visit in the following year. The large magnitude of cost estimates suggested that the IV assumption of local area depression diagnosis styles being unrelated to unmeasured confounders or outcomes might not be fulfilled. Therefore, estimate interpretations in the IV analysis and causal inferences between depression diagnosis rates and outcomes require caution.

We created ADR-based instruments as measures of local area depression diagnosing style that was theorized to be strongly related to depression diagnosis decisions, but unrelated to unmeasured confounders or outcomes. As shown in Figure 5.1, relatively low and high adjusted depression diagnosis rates spread out in the northeastern maps based on ADR-based instruments. This substantial variation in depression diagnosis illustrated in the maps served as the basis of our instrument for IV analysis. Previous research has shown that local area practice styles identified by the DACC method often described more treatment variation than alternative measures, such as using primary care service areas (PCSA).[96] Therefore, we selected ADR-based instruments using the DACC method.

One testable conjecture in IV analysis is that the instrument is strongly related to treatment choices. We assessed whether the ADR-based instruments described substantial variation in depression diagnosis across the United States. First, moving from the 1st to the 5th ADR quintile groups, depression diagnosis rates statistically significantly increased from 3.2% to 9.0% (Table 5.7). Of note, this is the variation in depression diagnosis that was explored for IV analyses. We examined the average effects of

depression diagnosis on health and economic outcomes when depression diagnosis rates changed between 3.2% and 9.0%.

Second, in the first stage of IV estimation, the Chow-F values for ADR-based instrument groups decreased as local areas expanded. This is consistent with previous research assessing the effect of area size when using local area practice style as an instrument.[223] Brooks et al. showed that using larger local areas to measure practice styles generate less treatment variation (larger Chow-F values) with larger standard errors of treatment estimates.[223] Brooks et al. also suggested that use of larger area sizes may mitigate the bias that local area practice style might be related to ecological factors within smaller areas (e.g. neighborhood cultural and behavioral factors).[223] However, it is been argued that physician practice styles around individual ZIP codes might have little in common in too large local areas.[96] Therefore, we tested the robustness of our IV models based on instruments of local depression diagnosing styles across different sizes with the minimum number of patients varying from 50 to 200 persons around each ZIP code (Appendix 1-39). We found consistent IV estimates across these instrument specifications in terms of significance and direction, but these estimates increased as local areas were expanded especially for healthcare costs. In the first stage of IV analysis, all Chow-F values greater than 10 (Table 5.8) indicated that our instruments described a significant portion of variation in depression diagnosis.

In a further investigation of using a 500-person local area, we found much larger IV estimates of depression diagnosis on healthcare costs than smaller areas. For example, an additional depression diagnosis within 30 days after AMI admission was found to be related to an average of a $52926 increase in 1-year total healthcare costs, which is about 5 times as much as using 50-person area ($9767) and 3 times as much as using 150-person area ($22517). For the 500-person areas, on average, it took about 1 hour and 20 minutes driving from each ZIP code and 158 ZIP codes to find sufficient patients, compared with only 32 minutes and 18 ZIP codes for 50-person areas and 49 minutes and

50 ZIP codes for 150-person areas. The larger geographic areas might have included many patients residing in a local area where physicians did not share common depression diagnosis styles and the ADR only reflected an average practice style of depression diagnosis. Brooks et al. indicated that the confounding issues might also exist in the large geographic areas.[223] Therefore, we carried out additional analyses to compare measures of patient overall health and physical functional status in charts across the ADR quintile groups for 500-person areas. Patients in the highest ADR quintile group of 500-person areas were more likely to have dementia during the index AMI hospitalization than those in the lowest group, compared with the distribution across ADR groups of 150-person areas. About 60-80% of patients with dementia have Alzheimer's disease that is the most expensive condition in the United States and Medicare is estimated to cover $113 billion in 2014.[224] As a result, more patients with dementia in the higher ADR quintile groups might contribute to a substantial portion of higher healthcare costs than those in the lower ADR quintile groups, which in turn, led to the large IV estimates of depression diagnosis on healthcare costs based on instruments of local area depression diagnosis styles.

The assumption underlying IV estimators is that the instrument is not related directly to outcomes or unmeasured confounders. As shown in Table 5.7, patient characteristics were more balanced across ADR-based instrument groups than depression diagnosis groups using Medicare claims data. Further evaluation of patient physical function and overall health that were unmeasured in claims but measured in charts revealed that measures of difficulties with ADL, ACE-27, AMI severity, and mental conditions were more evenly distributed across the ADR quintile groups than across depression diagnosis groups for a convenience sample (Table 5.14). However, patients in a higher ADR quintile group tended to have increased incontinence/elimination difficulties and to use a wheelchair. Furthermore, significant increasing trends of 1-year total healthcare costs, Part A, B (mostly physician fee schedule costs), and D costs moving from areas with less stronger physician preferences to diagnosing depression

measured by ADRs to stronger preferences. The increasing trend was also shown in 1-year outpatient visits post 30 days of the index AMI admission. In the 2nd stage of IV estimation, Hansen over-identification F test indirectly examined the IV assumption that ADR-based instruments did not have direct relationships with outcomes (Table 5.8). The Hansen over-identification F tests were insignificant, suggesting that the outcomes did not show direct relationships with the ADR-based instruments, except for prescription claims in the 30-day observation window, hospitalizations, ED visits, and outpatient visits in the 60-day observation window, and outpatient visits in the 90-day observation window. Given the correlations of the ADR-based instruments with our outcomes and some unmeasured confounders using hospital charts data and the Hansen over-identification F tests, our IV estimates based on ADR quintile groups might be biased toward worse survival and higher healthcare costs and utilization and the true effects of depression diagnosis might be better on survival and lower on healthcare costs and utilization.

The IV estimates of depression diagnosis on healthcare costs and utilization were almost implausibly large to represent only the extra costs associated with higher depression diagnosis rates across ADR quintile groups. Three possible reasons may explain why we observed the large IV estimates. First, it might be that local practice styles of depression diagnosis were highly related to healthcare utilization beyond depression care. In other words, areas with stronger physician preferences to diagnose depression might also have higher healthcare utilization in general. We further investigated whether our instruments based on local area practice style of depression diagnosis were related to local Medicare spending as a proxy of overall healthcare utilization. To obtain information on local Medicare spending, we used data from Dartmouth Atlas of Health Care online.[178] The Medicare spending was calculated as age, sex, and race adjusted Medicare reimbursement rates across hospital service areas (HSAs) using Medicare fee-for-service claims in 2006. We found a statistically

significant relationship between Medicare spending and ADR-based instruments with 150-person local area (Pearson correlation coefficient = 0.14, $p < 0.01$). Furthermore, the substantial increase in physician visits associated with higher depression diagnosis rates might have increase the opportunities for physician and patient interaction, which might lead to higher chance of disease detection and healthcare use. This suggested that our instruments of local area depression diagnosis styles might also incorporate general practice styles in the local areas that contributed to the large IV estimates of depression diagnosis on healthcare costs and utilization.

Second, it might be that patients living in areas with strong preferences of depression diagnosis need more care, which in turn, increased healthcare costs and utilization. Prior research suggested that mental problems could increase the complexity of patient medical care, and thereby increased healthcare costs and utilization.[225-228] As a result, in areas with stronger physician preferences of depression diagnosis, patients might actually indeed need more care for mental health and other medical conditions after the index hospitalization and depression diagnosis. We used chart abstracted data from a convenience sample attempting to measure patient overall health and physical functional statuses and did find an upward trend of using wheelchairs and incontinence/elimination difficulties, even though the differences across patients grouped by local area depression diagnosis styles were not statistically significant and much smaller than the differences across the depression diagnosis groups. Therefore, patients living in areas with strong physician preferences of diagnosing depression might actually need more professional help from the healthcare system than those in areas with less strong preferences, thereby had much higher healthcare costs and utilization. A further investigation was also carried out to examine whether patients used much more depression-related treatments after the index AMI admission. We found, on average, an AMI patient only had 0.014 psychotherapy services and 0.244 antidepressant claims within 1 year after the index admission. Clearly, the substantial increased costs associated

with higher depression diagnosis rates was not likely to result from the increased mental health treatments. This is consistent with previous studies in which treatments for other medical conditions accounted for a large proportion of healthcare costs for depressed patients.[4, 6] Patients with a depression diagnosis might need not only sufficient and appropriate depression care, but also treatments for other health problems.

Third, it is possible that local area depression diagnosis styles were highly related to local physician supply that contribute to high healthcare costs in that local area. As discussed in the theoretical model and previous research,[192, 229] areas with a higher supply of physicians and fewer patients per physician (e.g., more cardiologists, general practitioners, and psychiatrists in local areas) might be more likely to make a depression diagnosing decision with increased net utility via leisure time and income. With more physicians (fewer patients per physician) in a local area, physicians might have more time to spend with individual patients and evaluate their mental and physical conditions. As a result, in areas with higher physician supply, physicians might be more likely to diagnose more depression and recognize other mental and physical problems than those in areas with lower physician supply, which in turn, led to higher healthcare costs and utilization.

To obtain information on local physician supply, we used 2006 Medicare Physician Identification and Eligibility Records (MPIER) file that contains one record for each practice setting for a physician. With MPIER data, the total number of physicians was calculated across each ZIP code in the United States. Using the DACC method, the average driving time around each ZIP code was about 50 minutes for 150-person area size. Therefore, for physician supply measures across local areas, we drew a circle around each ZIP code to get a 50-minute driving area. Then, we extracted 2000 Census data to obtain information on the number of residents in each ZIP code. As a result, local area physician supply was calculated as the number of physicians divided by the number of residents in each ZIP code.

The Pearson correlation coefficient between the ADR-based instruments and local physician supply was 0.03 ($p < 0.01$), suggested that local area depression diagnosis styles had a very weak relationship with local physician supply. A closer inquiry was also made to assess whether there were correlations between physician supply for all specialty types and instruments. Using the same algorithm, we created local physician supply for general practitioners, cardiologists, and psychiatrists. Similarly, small Pearson correlation coefficients were found for both general practitioners and psychiatrists (0.03, $p < 0.01$), but not for cardiologists (<0.01, p=0.11). This indicated that general practitioners and psychiatrists might be the ones who made depression diagnosis a little more often than cardiologists in practice. Cardiologists might primarily focus on patient cardiac symptoms and treatment plan given the limited time interacting with patients, while general practitioners and psychiatrists spent more time with patients on evaluating general physical and mental health. Additionally, cardiologists might not feel confident in prescribing antidepressant medications as their training has focused on an entirely different body system.[46, 155, 160] Maybe, physician supply of general practitioners and psychiatrists in the local areas contributed a small proportion of local depression diagnosis styles that led to higher healthcare costs and utilization.

If patients need healthcare more in the local areas also with stronger physician depression diagnosis styles (measured by the ADR-based instruments) or higher physician supply than other areas, it was reasonable to observe substantial increases in healthcare costs and utilization associated with higher depression diagnosis rates from our IV analysis. It is possible that some other patient health outcomes, such as quality of life and depressive symptoms, improved significantly through higher healthcare utilization, but were not measured in this study. We think that our instruments based on local area depression diagnosis styles were related to the outcomes of healthcare costs and utilization and the IV estimates of depression diagnosis on healthcare costs and utilization might be biased toward high healthcare costs and utilization. Future research is

needed to search for instruments of local area practice styles that are not related to unmeasured confounders and outcomes to assess whether higher depression diagnosis rates lead to lower healthcare costs and utilization and improved depressive symptoms and quality of care.

Individual physician practice styles as instruments

The alternative instrument of this study was individual physician depression diagnosis styles measured by physician prior depression diagnosis behavior that was theorized to be strongly related to depression diagnosis, but unrelated to survival or healthcare costs and utilization. Specifically, we measured individual physician practice styles of depression diagnosis using a sample of AMI patients available that had consistent diagnosis information. Using a broader sample of patients than our analytical study sample to measure individual practice styles helps to ensure that our instrument measures are not based on idiosyncratic unmeasured characteristics of our AMI population. The IV estimates using individual physician depression diagnosis style as an instrument suggested that higher depression diagnosis rates would have decreased survival, increased patient healthcare costs (except Part D costs) and utilization of hospitalizations, ED, outpatient and physician services for patients whose depression diagnosis was affected by this instrument. For example, the estimate of depression diagnosis within 30 days after the index AMI admission on healthcare costs could be interpreted as an additional depression diagnosis associated with an average increase of $47861 of 1-year total healthcare costs for the marginal patients. In other words, a 1 percentage point increase in depression diagnosis rate for the entire study sample was associated with, on average, $478.61 increase in the total healthcare costs. However, the IV assumptions that individual physician depression diagnosis styles were unrelated to unmeasured confounders or outcomes might not be met in this analysis due to the implausible large cost estimates. Thus, our IV estimates of depression diagnosis might be biased toward worse survival and higher healthcare costs and utilization.

First, we assessed whether the instrument of individual physician depression diagnosis styles described substantial variation in depression diagnosis. Only 5.5% of patients were diagnosed with depression who saw physicians without giving a depression diagnosis in the past 6 months. In contrast, 10.9% of them were diagnosed with depression that saw physicians giving a depression diagnosis in the same timeframe. We assessed the average effects of depression diagnosis on health and economic outcomes when depression diagnosis rates changed between 5.5% and 10.9%. In addition, the first stage Chow-F values were all greater than 10, suggesting that our instruments based on individual physician depression diagnosis styles described a significant portion of variation in depression diagnosis.

Second, we examined whether the instrument based on individual physician depression diagnosis styles was not related to outcomes or unmeasured confounders. As shown in Table 5.10, similar distribution of patient characteristics were found across patients grouped by the instrument of individual physician depression diagnosis styles to across depression diagnosis groups. Patients seeing a physician who gave a depression diagnosis in the past 6 months were more likely to be sicker with more comorbidities prior to the index AMI admission.

Using a convenience sample of Medicare patients with AMI, our chart abstracted data showed a clear increasing trend for some measures for difficulties with activities of daily living across the instrument groups (personal hygiene/grooming, cane user, walker user, wheelchair user, and bed bound) moving from groups with less stronger individual physician preferences to depression diagnosis to those of stronger preferences. In addition, patients who saw physicians with stronger preferences of diagnosing depression were much more likely to have moderate and severe comorbidity evaluation. This suggested that our IV estimates based on individual practice styles estimates of depression diagnosis might be biased toward worse survival and higher healthcare costs and utilization.

Implications for theory

Based on a health production function and a utility-based theoretical model of physician diagnosing decision, this study explored variation in depression diagnosing across patients in practice to evaluate the health production function between depression diagnosis and patient health. Our theoretical model served as a conceptual tool to help portray the relationships among depression diagnosis, health outcomes, and factors affecting health and diagnosis.

We adopted our theoretical model to examining the effects of depression diagnosis on patient healthcare costs and utilization in IV analysis. We found that both instruments were related to outcomes of healthcare costs and utilization. In other words, patients with higher healthcare costs and utilization were more likely to reside in areas with strong preferences to depression diagnosis or to visit a physician with the strong preferences. It is possible that in local areas physicians with strong preferences of depression diagnosis also tended to have strong preferences of healthcare use in general, which led to high healthcare costs and utilization. Further investigation also illustrated that areas with strong preferences to diagnosing depression had slightly high physician supply. Physicians in areas with more competition would attempt to maximize their utility through providing more healthcare services.[192, 229] In this case, added depression diagnosis related to our instrument increased healthcare costs and utilization was probably related to all other healthcare services. Our instrument developed based on the theoretical model may be valid for clinical outcomes directly associated with a treatment or diagnosis, but not for broader outcomes associated with the whole healthcare system in a local area. Future research might need to expand the current theoretical model that serves as the basis for searching other instrument when investigating healthcare cost and utilization with depression diagnosis or a specific service.

Implications for methodology

With observational data, many health economists have employed the systematic analytical approach using alternative estimators with correct interpretations to assess whether the existing treatment rates are correct.[87, 88, 94-96, 113-118] However, as to our knowledge, little is known about whether this systematic approach could be applied to answering the "right" rate question for diagnosis. RCTs randomly assign patients to treatment groups and are considered to be the gold standard for clinical research. Still, knowledge gaps with regard to the effects of diagnosis in real-world settings can never be fulfilled using RCTs alone. This study used AMI patients as an example to demonstrate how to apply this systematic analytical approach to assessing whether the existing diagnosis rates are "right".

First, we used Medicare claims data with a large sample of AMI patients to obtain RA and IV estimates of depression diagnosis on patient survival and healthcare costs/utilization in real-world practice. Given the idea that treatment effects vary across patients with a given condition (treatment-effect heterogeneity), it is critically important to interpret RA and IV estimates for different subsets of patients, regardless of unmeasured confounders.[87, 88, 165-167] Our study findings of RA estimates of depression diagnosis on outcomes only applied to patients diagnosed with depression, while the IV estimates showed the effects of depression diagnosis for patients whose depression diagnosis was affected by the instruments selected. Then, using available measured patient characteristics in Medicare claims data and hospital chart abstracted data for a convenience sample, we attempted to assess the bias directions of our RA and IV estimates in the first step. As researchers criticized observational data, some important factors that affecting both treatment decision and clinical and economic outcomes were not measured when the data were collected.[98] Consequently, additional information on the unmeasured confounders were needed to help determine the bias directions of estimates obtained in observational data.

For example, this study theorized that patient depression severity, overall health, and physical functional status affected both depression diagnosis decision and outcomes, but they were not measured in Medicare claims data. The information on unmeasured confounders with accurate measures would be ideal if based on the entire population or a randomly selected sample, but this is not always practical. In this study, we used a convenience sample of patients with chart abstracted data to obtain additional information on the proxy measures of overall health, physical functional status. The information from chart abstracted data was used to identify if the unmeasured factors from claims-based datasets was evenly distributed across the diagnosis groups (RA assumption) and instrument groups of local area depression diagnosis styles (IV assumption).

In this study, using Medicare claims data, RA estimates showed depression diagnosis was associated with lower survival and higher healthcare costs and utilization for AMI patients diagnosed with depression, whereas IV estimates showed higher depression diagnosis rates were associated with higher healthcare costs, higher physician visits, but decreased ED visits and prescription drug claims for the marginal patients whose depression diagnosis was affected by the instruments of local physician depression diagnosis styles. Using the chart abstracted data for a convenience sample we found patients diagnosed with depression tended to have worse physical functional status (difficulties with ADLs), comorbidities (ACE-27), and mental illnesses during the index AMI hospitalization than the undiagnosed patients. Therefore, our RA estimates of depression diagnosis might be biased toward worse survival and higher healthcare costs and utilization. Across patients grouped by local physician depression diagnosis styles, the measured factors in charts were more evenly distributed than those across the diagnosis groups. However, we did found an upward trend of some difficulties of ADL (using a walker and wheelchair) from areas with less stronger physician preferences of depression diagnosis to those with stronger preferences. Further investigation revealed

the correlations of local depression diagnosis styles with preferences of healthcare use in general and with local physician supply, which suggested that our IV estimates of depression diagnosis might be biased toward higher healthcare costs and utilization. Future research could adopt this systematic analytical approach to assessing the question of "which rate is right?" with a valid instrument or with more clinically relevant outcomes such as improvement of depressive symptoms or patient quality of life.

Implications for practice

Application of our study findings to practice on the issue of over- or under-diagnosis of depression requires caution, especially with the implausibly higher healthcare costs associated with additional depression diagnosis from the IV analysis. Using both Medicare claims data, we showed that our instrument of local area depression diagnosis styles was strongly related to depression diagnosis decisions. We further revealed local area depression diagnosis styles might be correlated with preferences of healthcare use in general and physician supply in the local areas, which in turn, led to the implausible higher healthcare costs.

Given these correlations, we still found that additional depression diagnosis was associated with statistically significant decrease in ED visits and prescription claims within 1 year after the index AMI admission. We think that relative to the true effects, IV estimates of the effects of depression diagnosis might be biased low on ED visits and prescription claims. Therefore, in practice, if physicians increased the awareness of patient depressive symptoms and evaluate their mental health, additional depression diagnosis with following appropriate treatment would have decreased ED visits, the most expensive healthcare utilization. In addition, increasing attention has been drawn to the widely reported issue of polypharmacy (taking multiple medications) in the elderly that is associated with greater healthcare costs and increased risks of adverse drug events, medication non-adherence, and decreased functional capability.[230-232] Our IV analysis also showed that additional depression diagnosis was associated with more physician

visits. More frequent contacts with physicians might partially result in lower ED visits and more opportunities to detect inappropriate medication use, which in turn, might contribute to improved patient quality of life and reduced healthcare expenditures in the long term. The high healthcare costs and increased physician visits associated with higher depression diagnosis rates might improve patient depressive symptoms and quality of life and slow disease progression substantially. However, using Medicare claims data, we were not able to capture patient depressive symptoms, quality of life and other clinical outcomes closely related to depression diagnosis. Future research is needed to investigating whether higher rates of depressions diagnosis affect depressive symptoms and quality of life in practice.

Healthcare policy attention has also been drawn to improving patient health outcomes in primary care settings when mental illness is frequently reported to be under-diagnosed and under-treated in the elderly.[233] Starting from October 14, 2011, the Centers for Medicare & Medicaid Services (CMS) cover an annual screening for depression for Medicare beneficiaries in primary care settings through Medicare Part B plan, so that depressed patients could be diagnosed early and accurately with effective treatment and follow-up visits. Our study showed that patients diagnosed later after AMI admission were also more likely to have more comorbidities and higher healthcare costs and utilization. With the new national coverage of depression screening by Medicare Part B, elderly patients with depression, including those sicker patients with higher healthcare utilization, would have the opportunity to have early evaluation of their mental health and effective treatment plan to slow disease progression, improve health outcomes, and control healthcare cost in the long term.

Limitations

We acknowledge several important limitations in this study. First, the estimates of depression diagnosis on outcomes were only applicable to the subsets of patients because of treatment-effect heterogeneity. For example, the IV estimates based on local area

practice styles were restricted to depression rates between 3.2% and 9.0% for AMI patients. Second, this study sample was restricted to Medicare patients under fee-for-service system who met our inclusion criteria, thereby limiting generalizability to Medicare populations in managed care system or other younger populations. A comparison between the analytical sample and the excluded Medicare patients revealed that patients in our sample were more likely to be younger and female, and to live in areas with fewer neighborhood problems and higher walkability. Thus, we expected the effects of depression diagnosis would be toward worse health outcome and higher healthcare costs and utilization for the excluded patients. Third, with limited information on patient health outcomes, we were not able to measure patient health outcomes of depressive symptoms or quality of life. It is possible that additional depression diagnosis led to higher healthcare costs and utilization within 1 year after AMI admission because patients had more chances to have direct contacts with healthcare providers and more services could be provided promptly. However, the increased costs and utilization of healthcare might have resulted in improved patient depressive symptoms or quality of life that was not measured in Medicare claims data or our charts. Future research is needed to incorporate patient depressive symptoms and quality of life measures into analyzing the effects of depression diagnosis on health outcomes. Forth, our chart abstracted data was from a convenience sample of AMI patient that might not be representative of our study sample. No depressive symptoms were recorded in the abstracted data that made it difficult to directly assess patient depression severity across depression diagnosis groups or patients grouped by local area or individual depression diagnosis styles. Lastly, we only evaluated patient survival, healthcare costs and utilization for 1 year after AMI admission. Maybe depression diagnosis gradually affected these outcome measures. Even though we observed decreased survival, increased healthcare costs and utilization associated with additional depression diagnosis, except ED visits, it is possible,

increasing depression diagnosis rates might have improved patient health outcomes and decreased healthcare cost or utilization in a longer timeframe.

Conclusion

We found substantial variation in local area practice styles of depression diagnosis measured by area diagnosis ratios across the United States using the DACC method. Our instrument of local area depression diagnosis styles was significantly associated with depression diagnosis for AMI patients. The association between depression diagnosis and the alternative instrument of individual physician practice styles of depression diagnosis was also identified in our study.

After adjusting for patient demographic characteristics, comorbidities, procedure and therapy, medical use, and contextual factors, our RA estimates showed that depression diagnosis significantly decreased survival within 1 year after the index AMI admission date, but increased healthcare costs and utilization for AMI patients diagnosed with depression. The RA estimates might be biased toward worse health outcomes and higher healthcare costs and utilization due to unmeasured confounders and early recognition of depression followed by appropriate treatments might benefit the diagnosed patients more than late detection and treatments. Our IV estimates suggested that additional depression diagnosis was associated with increased healthcare costs and physician visits, but decreased ED visits and prescription claims for the marginal patients. However, our instruments based on local physician depression diagnosis styles might be correlated with local area practice styles in general (preference to healthcare utilization overall) and local physician supply, and thereby affect healthcare utilization and costs. Therefore, our instruments might not be valid and we cannot conclude whether the existing depression diagnosis rates need to be changed. Future research using alternative instruments that are not directly related to outcomes or unmeasured confounders is needed to help answer whether the existing diagnosis rates are correct.

APPENDIXA

SENSITIVITY ANALYSIS

Table A1. Instrumental variables estimates of the effectiveness of depression diagnosis on survival for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.05	0.03	0.13	-0.05*	0.03	0.09	-0.06*	0.03	0.06
60	-0.06	0.04	0.12	-0.07**	0.03	0.04	-0.06*	0.03	0.08
70	-0.07*	0.04	0.07	-0.06*	0.04	0.08	-0.06*	0.04	0.10
80	-0.09**	0.04	0.03	-0.09**	0.04	0.02	-0.08**	0.04	0.04
90	-0.08*	0.04	0.06	-0.08*	0.04	0.06	-0.07*	0.04	0.10
100	-0.05	0.05	0.23	-0.07	0.04	0.11	-0.05	0.04	0.23
110	-0.05	0.05	0.30	-0.05	0.04	0.28	-0.04	0.04	0.38
120	-0.04	0.05	0.47	-0.03	0.05	0.52	-0.03	0.04	0.50
130	-0.04	0.05	0.42	-0.02	0.05	0.66	-0.03	0.05	0.56
140	-0.05	0.05	0.33	-0.01	0.05	0.81	-0.03	0.05	0.54
150	-0.03	0.05	0.57	0.00	0.05	0.96	-0.01	0.05	0.91
160	-0.04	0.05	0.44	-0.03	0.05	0.53	-0.03	0.05	0.60
170	-0.02	0.06	0.76	-0.02	0.05	0.66	-0.01	0.05	0.78
180	-0.02	0.06	0.68	-0.01	0.05	0.81	-0.01	0.05	0.88
190	-0.03	0.06	0.61	-0.01	0.05	0.85	0.00	0.05	0.93
200	-0.02	0.06	0.72	0.00	0.06	1.00	-0.01	0.05	0.88

Notes:

ADR: area diagnosis ratio;

Table A1. Continued

Notes:

Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;
All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Survival was set to 1 if a patient survived the first year after the index AMI admission, 0 otherwise.

Table A2. Instrumental variables estimates of the effectiveness of depression diagnosis on total healthcare costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	9767.30**	2642.24	<0.01	12743.47**	2490.71	<0.01	13152.41**	2404.95	<0.01
60	13560.60**	2826.08	<0.01	14056.98**	2657.95	<0.01	15294.76**	2594.02	<0.01
70	12583.10**	2944.39	<0.01	15300.91**	2800.31	<0.01	15144.15**	2715.81	<0.01
80	15219.14**	3143.32	<0.01	16248.97**	2985.85	<0.01	16374.24**	2887.51	<0.01
90	14222.93**	3314.09	<0.01	15081.24**	3136.96	<0.01	16970.08**	3057.28	<0.01
100	15541.61**	3491.56	<0.01	16706.29**	3277.69	<0.01	18457.60**	3212.55	<0.01
110	17765.75**	3650.32	<0.01	20103.96**	3447.02	<0.01	19638.36**	3352.59	<0.01
120	17080.11**	3723.20	<0.01	19862.21**	3517.92	<0.01	19799.85**	3423.74	<0.01
130	21532.15**	3837.39	<0.01	21602.17**	3623.22	<0.01	21651.33**	3520.56	<0.01
140	22380.58**	4000.29	<0.01	20845.47**	3733.12	<0.01	22211.03**	3651.31	<0.01
150	22516.93**	4046.17	<0.01	20723.66**	3805.74	<0.01	23042.75**	3690.37	<0.01
160	24607.51**	4170.97	<0.01	23509.40**	3884.01	<0.01	24941.07**	3802.87	<0.01
170	25344.58**	4276.80	<0.01	23485.03**	3972.50	<0.01	24694.28**	3895.35	<0.01
180	28674.22**	4368.91	<0.01	27301.49**	4074.01	<0.01	28309.86**	4021.95	<0.01
190	31572.95**	4506.61	<0.01	29261.27**	4144.70	<0.01	31107.23**	4074.36	<0.01
200	32603.75**	4640.43	<0.01	32602.68**	4289.14	<0.01	32517.14**	4174.55	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A2. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Table A3. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part A costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	6320.94**	2061.17	<0.01	7982.75**	1953.70	<0.01	8255.66**	1881.04	<0.01
60	9561.22**	2210.15	<0.01	9466.46**	2082.00	<0.01	10472.31**	2034.06	<0.01
70	8632.92**	2303.31	<0.01	10126.09**	2186.72	<0.01	9878.85**	2127.36	<0.01
80	9567.43**	2453.39	<0.01	10371.87**	2328.09	<0.01	10474.96**	2259.39	<0.01
90	9256.79**	2590.87	<0.01	9217.83**	2447.02	<0.01	10548.21**	2393.58	<0.01
100	9118.62**	2727.64	<0.01	10266.87**	2559.76	<0.01	11441.31**	2516.41	<0.01
110	10776.15**	2849.26	<0.01	12025.32**	2682.31	<0.01	11881.48**	2613.00	<0.01
120	9576.46**	2905.15	<0.01	11548.16**	2742.73	<0.01	12094.48**	2666.17	<0.01
130	12397.02**	3006.89	<0.01	13144.69**	2836.16	<0.01	13175.22**	2760.44	<0.01
140	13561.02**	3116.35	<0.01	12893.88**	2925.26	<0.01	13529.52**	2857.21	<0.01
150	13452.63**	3168.62	<0.01	12463.60**	2979.91	<0.01	13902.39**	2882.83	<0.01
160	14515.60**	3260.90	<0.01	14314.58**	3037.79	<0.01	15004.33**	2966.62	<0.01
170	15275.28**	3341.64	<0.01	14025.13**	3105.21	<0.01	14717.96**	3041.51	<0.01
180	16879.02**	3409.39	<0.01	16522.31**	3177.96	<0.01	17736.41**	3137.16	<0.01
190	19114.25**	3496.23	<0.01	17824.93**	3224.80	<0.01	19196.66**	3168.90	<0.01
200	19348.42**	3593.66	<0.01	19996.31**	3334.38	<0.01	19925.43**	3242.22	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A3. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part A costs summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30days) or till death;

Table A4. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part B costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	3095.48**	942.90	<0.01	4119.32**	854.23	<0.01	4383.60**	827.59	<0.01
60	3548.94**	997.29	<0.01	3980.08**	917.98	<0.01	4285.34**	890.33	<0.01
70	3526.69**	1037.35	<0.01	4540.92**	994.12	<0.01	4700.02**	942.15	<0.01
80	5139.71**	1108.84	<0.01	5147.39**	1062.72	<0.01	5285.07**	1005.49	<0.01
90	4476.75**	1163.83	<0.01	5145.98**	1117.32	<0.01	5733.66**	1064.41	<0.01
100	5832.58**	1233.27	<0.01	5565.31**	1157.99	<0.01	6180.55**	1112.67	<0.01
110	6204.59**	1293.24	<0.01	6886.37**	1228.76	<0.01	6637.94**	1196.12	<0.01
120	6599.09**	1319.76	<0.01	7092.75**	1243.26	<0.01	6642.89**	1222.35	<0.01
130	8064.25**	1298.48	<0.01	7327.74**	1240.31	<0.01	7340.80**	1189.25	<0.01
140	7869.75**	1400.29	<0.01	6993.16**	1271.86	<0.01	7659.13**	1240.18	<0.01
150	8143.95**	1369.57	<0.01	7452.22**	1300.81	<0.01	8112.45**	1263.47	<0.01
160	9125.26**	1421.75	<0.01	8475.46**	1323.74	<0.01	9062.08**	1299.80	<0.01
170	9005.99**	1451.46	<0.01	8590.94**	1356.14	<0.01	8997.94**	1329.41	<0.01
180	10634.82**	1489.17	<0.01	9762.35**	1392.88	<0.01	9535.89**	1368.30	<0.01
190	11623.96**	1581.53	<0.01	10248.83**	1417.31	<0.01	10710.85**	1392.72	<0.01
200	12184.03**	1625.74	<0.01	11425.22**	1464.27	<0.01	11446.02**	1428.97	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A4. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B costs summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30 days) or till death;

Table A5. Instrumental variables estimates of the effectiveness of depression diagnosis on Part B outpatient costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-221.61	581.67	0.70	159.09	489.97	0.75	333.60	459.75	0.47
60	-225.06	612.12	0.71	-117.82	551.21	0.83	-21.01	526.54	0.97
70	-485.62	629.48	0.44	-214.21	623.75	0.73	-40.18	559.28	0.94
80	-230.93	675.04	0.73	-96.29	668.69	0.89	-45.35	603.73	0.94
90	-601.59	717.46	0.40	-75.87	703.28	0.91	153.02	645.01	0.81
100	-122.78	756.38	0.87	-145.99	712.73	0.84	34.28	663.96	0.96
110	-312.24	795.12	0.70	291.30	769.60	0.71	11.89	757.33	0.99
120	42.56	812.29	0.96	550.92	762.00	0.47	45.44	770.51	0.95
130	897.92	722.16	0.21	489.62	710.57	0.49	489.02	668.27	0.46
140	952.48	837.35	0.26	513.24	732.59	0.48	702.76	699.03	0.32
150	861.34	765.79	0.26	726.39	747.97	0.33	869.68	707.33	0.22
160	1078.88	778.90	0.17	834.53	741.76	0.26	1059.00	719.21	0.14
170	594.91	801.89	0.46	837.92	761.42	0.27	939.42	733.60	0.20
180	1089.76	815.69	0.18	1301.88*	772.59	0.09	1136.93	754.77	0.13
190	1595.22*	911.51	0.08	1099.81	779.72	0.16	1381.32*	764.09	0.07
200	1797.62*	937.27	0.06	1580.72**	807.94	0.05	1662.82**	788.45	0.04

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A5. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B outpatient costs summed up all standardized payments from outpatient claims over the 1 year period post (the index date + 30 days) or till death;

Table A6. Instrumental variables estimates of the effectiveness of depression diagnosis on Part B physician fee schedule costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	2583.11**	367.75	<0.01	2949.37**	347.82	<0.01	3062.44**	339.43	<0.01
60	2978.54**	395.43	<0.01	3283.73**	374.41	<0.01	3408.98**	366.44	<0.01
70	3285.97**	413.77	<0.01	3774.66**	394.67	<0.01	3753.45**	386.81	<0.01
80	4180.13**	447.83	<0.01	4176.31**	423.73	<0.01	4279.73**	413.48	<0.01
90	4177.68**	471.84	<0.01	4388.08**	446.25	<0.01	4636.50**	438.41	<0.01
100	4669.66**	497.14	<0.01	4691.81**	468.07	<0.01	4999.08**	463.03	<0.01
110	5372.39**	528.32	<0.01	5371.00**	495.75	<0.01	5531.20**	485.00	<0.01
120	5263.60**	535.47	<0.01	5458.09**	508.78	<0.01	5633.36**	497.44	<0.01
130	5848.00**	559.32	<0.01	5790.70**	526.66	<0.01	5735.69**	515.09	<0.01
140	5670.13**	578.72	<0.01	5739.51**	544.15	<0.01	6015.10**	536.54	<0.01
150	6029.48**	590.47	<0.01	5887.32**	557.56	<0.01	6141.25**	544.36	<0.01
160	6462.23**	611.49	<0.01	6384.69**	576.23	<0.01	6632.16**	565.45	<0.01
170	7085.51**	634.17	<0.01	6724.84**	590.59	<0.01	6780.34**	579.44	<0.01
180	7667.07**	652.92	<0.01	7077.74**	608.13	<0.01	7161.31**	600.16	<0.01
190	8098.11**	673.54	<0.01	7614.64**	622.88	<0.01	7788.43**	615.21	<0.01
200	8307.80**	693.04	<0.01	8103.52**	647.98	<0.01	8124.94**	632.00	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A6. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B physician fee schedule costs summed up all standardized payments from standardized carrier and durable medical equipment claims for physician fee schedules over the 1 year period post (the index date + 30 days) or till death;

Table A7. Instrumental variables estimates of the effectiveness of depression diagnosis on other Part B costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	733.98**	381.07	0.05	1010.866**	359.69	0.01	987.557**	364.37	0.01
60	795.455**	401.59	0.05	814.168**	358.78	0.02	897.371**	354.30	0.01
70	726.35*	423.45	0.09	980.470**	383.60	0.01	986.744**	376.22	0.01
80	1190.515**	437.80	0.01	1067.371**	407.21	0.01	1050.693**	394.08	0.01
90	900.665**	449.50	0.05	833.77**	426.09	0.05	944.144**	412.25	0.02
100	1285.693**	483.62	0.01	1019.491**	453.18	0.02	1147.185**	437.73	0.01
110	1144.441**	502.12	0.02	1224.073**	464.20	0.01	1094.848**	450.05	0.02
120	1292.933**	509.44	0.01	1083.742**	474.76	0.02	964.091**	456.74	0.04
130	1318.333**	524.35	0.01	1047.424**	494.00	0.03	1116.086**	475.40	0.02
140	1247.140**	545.38	0.02	740.42	501.34	0.14	941.27*	496.32	0.06
150	1253.134**	549.05	0.02	838.52*	512.71	0.10	1101.520**	511.58	0.03
160	1584.149**	598.70	0.01	1256.243**	527.83	0.02	1370.920**	525.49	0.01
170	1325.566**	587.99	0.02	1028.19*	540.70	0.06	1278.171**	542.57	0.02
180	1877.998**	603.58	<0.01	1382.730**	562.24	0.01	1237.652**	555.87	0.03
190	1930.638**	623.53	<0.01	1534.378**	576.36	0.01	1541.093**	564.53	0.01
200	2078.620**	634.65	<0.01	1740.985**	581.62	<0.01	1658.259**	569.26	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A7. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Other Part B costs summed up all standardized payments from standardized carrier and durable medical equipment claims for non-physician fee schedules, including ambulatory surgery center, durable medical equipment, anesthesia, prosthetics, orthotics, lab, drugs, and ambulance over the 1 year period post (the index date + 30 days) or till death;

Table A8. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part D costs for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	350.89	291.39	0.23	641.392**	261.88	0.01	513.155**	252.28	0.04
60	450.44	310.57	0.15	610.443**	275.84	0.03	537.110**	270.11	0.05
70	423.49	324.32	0.19	633.906**	289.60	0.03	565.290**	284.52	0.05
80	511.99	326.24	0.12	729.716**	306.70	0.02	614.202**	295.55	0.04
90	489.39	342.92	0.15	717.428**	326.28	0.03	688.212**	312.52	0.03
100	590.42*	361.07	0.10	874.106**	344.74	0.01	835.743**	33<0.01	0.01
110	785.021**	372.18	0.04	1192.268**	358.05	<0.01	1118.936**	344.26	<0.01
120	904.564**	380.85	0.02	1221.298**	367.70	<0.01	1062.474**	351.58	<0.01
130	1070.878**	398.73	0.01	1129.740**	376.13	<0.01	1135.314**	362.58	<0.01
140	949.815**	417.12	0.02	958.428**	388.92	0.01	1022.385**	380.94	0.01
150	920.354**	421.89	0.03	807.831**	398.26	0.04	1027.907**	384.71	0.01
160	966.653**	435.16	0.03	719.36*	407.95	0.08	874.657**	393.87	0.03
170	1063.315**	444.47	0.02	868.955**	417.03	0.04	978.390**	404.42	0.02
180	1160.377**	453.76	0.01	1016.839**	429.13	0.02	1037.557**	417.35	0.01
190	834.74*	461.74	0.07	1187.511**	437.98	0.01	1199.719**	421.56	<0.01
200	1071.303**	476.33	0.03	1181.149**	442.89	0.01	1145.690**	430.68	0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A8. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part D costs summed up all standardized payments from Part D prescription drug claims over the 1 year period post (the index date + 30 days) or till death;

Table A9. Instrumental variables estimates of the effectiveness of depression diagnosis on hospitalizations for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	0.10	0.14	0.46	0.15	0.13	0.25	0.20	0.13	0.13
60	0.22	0.15	0.13	0.22	0.14	0.12	0.25*	0.14	0.07
70	0.19	0.16	0.23	0.31**	0.15	0.04	0.25*	0.14	0.09
80	0.19	0.17	0.27	0.28*	0.16	0.08	0.24	0.15	0.11
90	0.09	0.18	0.63	0.15	0.17	0.36	0.22	0.16	0.17
100	0.03	0.18	0.88	0.16	0.17	0.35	0.22	0.17	0.19
110	0.20	0.19	0.29	0.29	0.18	0.11	0.26	0.18	0.14
120	0.14	0.20	0.47	0.20	0.19	0.28	0.23	0.18	0.21
130	0.28	0.20	0.17	0.36*	0.19	0.06	0.33*	0.19	0.08
140	0.25	0.21	0.23	0.29	0.20	0.14	0.33*	0.19	0.09
150	0.35*	0.22	0.10	0.26	0.20	0.19	0.33*	0.20	0.09
160	0.37*	0.22	0.09	0.38*	0.21	0.07	0.40**	0.20	0.05
170	0.32	0.23	0.16	0.36*	0.21	0.09	0.31	0.21	0.13
180	0.48**	0.23	0.04	0.54**	0.22	0.01	0.51**	0.21	0.02
190	0.50**	0.24	0.04	0.56**	0.22	0.01	0.54**	0.21	0.01
200	0.55*	0.24	0.03	0.62**	0.23	0.01	0.57**	0.22	0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A9. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30 days) or till death;

Table A10. Instrumental variables estimates of the effectiveness of depression diagnosis on ED visits for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.30*	0.18	0.10	-0.31*	0.17	0.06	-0.19	0.16	0.24
60	-0.14	0.19	0.46	-0.28	0.18	0.12	-0.24	0.17	0.17
70	-0.20	0.20	0.32	-0.18	0.19	0.34	-0.23	0.18	0.21
80	-0.31	0.21	0.15	-0.26	0.20	0.19	-0.32*	0.19	0.09
90	-0.35	0.22	0.12	-0.34	0.21	0.11	-0.33*	0.20	0.10
100	-0.37	0.23	0.12	-0.44**	0.22	0.04	-0.41**	0.21	0.05
110	-0.36	0.24	0.14	-0.41*	0.23	0.07	-0.53**	0.22	0.02
120	-0.56**	0.25	0.02	-0.54**	0.24	0.02	-0.57**	0.23	0.01
130	-0.38	0.26	0.14	-0.51**	0.24	0.04	-0.54**	0.23	0.02
140	-0.58**	0.27	0.03	-0.52**	0.25	0.04	-0.51**	0.25	0.04
150	-0.48*	0.28	0.08	-0.50**	0.26	0.05	-0.47*	0.25	0.06
160	-0.40	0.28	0.16	-0.49*	0.26	0.06	-0.49*	0.26	0.06
170	-0.57**	0.29	0.05	-0.58**	0.27	0.03	-0.63**	0.26	0.02
180	-0.38	0.29	0.20	-0.33	0.28	0.23	-0.45*	0.27	0.09
190	-0.34	0.30	0.26	-0.36	0.28	0.20	-0.38	0.27	0.17
200	-0.32	0.31	0.30	-0.31	0.28	0.28	-0.43	0.28	0.12

Notes:

ED: emergency department;
ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A10. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30days) or till death;

Table A11. Instrumental variables estimates of the effectiveness of depression diagnosis on outpatient visits for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-2.10**	0.75	0.01	-1.75**	0.71	0.01	-1.72**	0.68	0.01
60	-1.77**	0.80	0.03	-1.47**	0.75	0.05	-1.28*	0.72	0.08
70	-0.83	0.84	0.32	-0.82	0.78	0.30	-0.68	0.75	0.36
80	-1.98**	0.90	0.03	-0.50	0.84	0.55	-1.09	0.80	0.18
90	-1.77*	0.95	0.06	-1.02	0.88	0.25	-0.98	0.85	0.25
100	-0.62	1.00	0.53	-1.14	0.93	0.22	-0.96	0.89	0.28
110	-0.71	1.03	0.49	-0.67	0.97	0.49	-1.19	0.93	0.20
120	-0.33	1.05	0.76	0.14	0.99	0.89	-0.80	0.95	0.40
130	-0.78	1.08	0.47	-0.29	1.03	0.78	-0.47	0.98	0.63
140	-0.29	1.13	0.80	0.02	1.06	0.99	-0.55	1.02	0.59
150	-0.53	1.15	0.65	-0.36	1.07	0.74	-0.26	1.03	0.80
160	0.42	1.19	0.72	-0.30	1.10	0.79	-0.40	1.06	0.71
170	-0.14	1.21	0.91	-0.25	1.12	0.83	-0.14	1.09	0.90
180	0.53	1.24	0.67	0.56	1.15	0.62	0.49	1.11	0.66
190	0.21	1.27	0.87	0.36	1.16	0.76	0.40	1.12	0.72
200	0.59	1.30	0.65	-0.06	1.19	0.96	-0.07	1.14	0.95

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A11. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30days) or till death;

Table A12. Instrumental variables estimates of the effectiveness of depression diagnosis on physician visits for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	15.39**	1.85	<0.01	17.33**	1.75	<0.01	17.02**	1.70	<0.01
60	17.76**	2.00	<0.01	19.17**	1.90	<0.01	19.08**	1.85	<0.01
70	19.01**	2.10	<0.01	21.27**	2.01	<0.01	20.66**	1.94	<0.01
80	22.89**	2.26	<0.01	22.55**	2.14	<0.01	22.68**	2.07	<0.01
90	24.15**	2.39	<0.01	22.81**	2.25	<0.01	23.89**	2.20	<0.01
100	26.12**	2.54	<0.01	25.68**	2.38	<0.01	26.59**	2.33	<0.01
110	29.07**	2.67	<0.01	28.62**	2.51	<0.01	29.04**	2.47	<0.01
120	28.04**	2.71	<0.01	29.15**	2.57	<0.01	29.68**	2.52	<0.01
130	31.48**	2.83	<0.01	30.85**	2.66	<0.01	29.58**	2.58	<0.01
140	30.94**	2.93	<0.01	32.04**	2.77	<0.01	31.71**	2.70	<0.01
150	32.57**	3.01	<0.01	32.01**	2.84	<0.01	32.24**	2.74	<0.01
160	35.17**	3.13	<0.01	33.52**	2.89	<0.01	34.26**	2.84	<0.01
170	36.79**	3.21	<0.01	34.70**	2.97	<0.01	35.26**	2.93	<0.01
180	39.71**	3.30	<0.01	36.54**	3.05	<0.01	37.36**	3.02	<0.01
190	41.30**	3.39	<0.01	39.11**	3.14	<0.01	39.60**	3.08	<0.01
200	43.32**	3.51	<0.01	41.25**	3.25	<0.01	40.44**	3.14	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A12. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Physician visits were based on the number of outpatient/carrier claims for evaluation and management services by physicians over the 1-year period post (the index date + 30days) or till death;

Table A13. Instrumental variables estimates of the effectiveness of depression diagnosis on prescription claims for elderly patients with acute myocardial infarction (30-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-6.78**	3.12	0.03	-4.93	2.95	0.10	17.02**	1.70	<0.01
60	-7.08**	3.34	0.03	-4.79	3.14	0.13	19.08**	1.85	<0.01
70	-8.56**	3.50	0.02	-6.29	3.29	0.06	20.66**	1.94	<0.01
80	-11.01**	3.73	<0.01	-10.52**	3.50	<0.01	22.68**	2.07	<0.01
90	-9.67**	3.93	0.01	-9.53**	3.69	0.01	23.89**	2.20	<0.01
100	-9.85**	4.11	0.02	-8.97*	3.87	0.02	26.59**	2.33	<0.01
110	-6.41	4.31	0.14	-6.68	4.02	0.10	29.04**	2.47	<0.01
120	-7.57*	4.39	0.09	-7.53	4.14	0.07	29.68**	2.52	<0.01
130	-8.00*	4.53	0.08	-7.97	4.30	0.06	29.58**	2.58	<0.01
140	-10.87**	4.73	0.02	-10.20*	4.44	0.02	31.71**	2.70	<0.01
150	-10.40**	4.82	0.03	-12.08**	4.53	0.01	32.24**	2.74	<0.01
160	-11.71**	4.97	0.02	-14.34**	4.63	<0.01	34.26**	2.84	<0.01
170	-12.59**	5.10	0.01	-14.57**	4.74	<0.01	35.26**	2.93	<0.01
180	-15.28**	5.19	<0.01	-13.35**	4.83	0.01	37.36**	3.02	<0.01
190	-22.54**	5.35	<0.01	-13.36**	4.89	0.01	39.60**	3.08	<0.01
200	-22.28**	5.49	<0.01	-16.06**	5.02	<0.01	40.44**	3.14	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A13. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30days) or till death;

Table A14. Instrumental variables estimates of the effectiveness of depression diagnosis on survival for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.06**	0.03	0.04	-0.08**	0.03	<0.01	-0.08**	0.03	<0.01
60	-0.08**	0.03	0.01	-0.07**	0.03	0.01	-0.07**	0.03	0.01
70	-0.08**	0.03	0.02	-0.09**	0.03	<0.01	-0.08**	0.03	0.01
80	-0.09**	0.04	0.01	-0.09**	0.03	0.01	-0.09**	0.03	0.01
90	-0.08**	0.04	0.03	-0.08**	0.04	0.02	-0.08**	0.03	0.01
100	-0.06*	0.04	0.10	-0.09**	0.04	0.01	-0.08**	0.04	0.03
110	-0.08*	0.04	0.06	-0.09**	0.04	0.02	-0.08**	0.04	0.03
120	-0.07	0.04	0.11	-0.07*	0.04	0.07	-0.09**	0.04	0.02
130	-0.07*	0.04	0.08	-0.07*	0.04	0.07	-0.09**	0.04	0.02
140	-0.08*	0.04	0.08	-0.05	0.04	0.21	-0.08**	0.04	0.05
150	-0.07*	0.05	0.10	-0.07*	0.04	0.09	-0.08*	0.04	0.06
160	-0.06	0.05	0.20	-0.07*	0.04	0.09	-0.07*	0.04	0.08
170	-0.07	0.05	0.15	-0.06	0.04	0.14	-0.06	0.04	0.17
180	-0.04	0.05	0.42	-0.04	0.04	0.32	-0.05	0.04	0.28
190	-0.06	0.05	0.19	-0.06	0.05	0.20	-0.07	0.04	0.11
200	-0.07	0.05	0.16	-0.03	0.05	0.46	-0.05	0.04	0.30

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A14. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Survival was set to 1 if a patient survived the first year after the index AMI admission, 0 otherwise.

Table A15. Instrumental variables estimates of the effectiveness of depression diagnosis on total healthcare costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	13323.06**	2175.55	<0.01	12454.32**	1996.20	<0.01	12365.27**	1944.39	<0.01
60	15242.37**	2298.89	<0.01	14759.45**	2129.07	<0.01	14480.49**	2074.45	<0.01
70	15931.06**	2463.91	<0.01	15275.29**	2289.95	<0.01	15268.28**	2230.74	<0.01
80	16154.76**	2569.91	<0.01	16622.56**	2451.52	<0.01	16811.73**	2368.02	<0.01
90	16956.98**	2709.47	<0.01	17438.86**	2598.23	<0.01	18455.89**	2517.60	<0.01
100	17304.64**	2839.42	<0.01	18411.96**	2710.00	<0.01	19336.01**	2631.62	<0.01
110	18447.56**	2961.35	<0.01	16965.71**	2780.30	<0.01	19058.957**	2717.67	<0.01
120	18533.70**	3034.33	<0.01	19487.95**	2901.02	<0.01	20049.92**	2778.43	<0.01
130	19361.96**	3100.67	<0.01	20248.73**	2958.87	<0.01	21790.73**	2834.58	<0.01
140	19825.78**	3239.41	<0.01	21909.67**	3012.48	<0.01	22197.96**	2884.63	<0.01
150	21138.34**	3330.57	<0.01	22166.13**	3085.10	<0.01	23393.72**	2987.26	<0.01
160	23174.96**	3493.59	<0.01	21447.00**	3142.15	<0.01	23406.92**	3067.32	<0.01
170	24115.61**	3500.58	<0.01	23643.00**	3284.38	<0.01	25463.57**	3206.34	<0.01
180	25639.49**	3529.43	<0.01	25563.90**	3344.48	<0.01	27322.92**	3238.23	<0.01
190	27899.19**	3619.83	<0.01	27479.45**	3426.86	<0.01	29263.59**	3279.71	<0.01
200	27329.42**	3651.34	<0.01	28736.44**	3508.38	<0.01	30202.61**	3385.38	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A15. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 60 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Table A16. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part A costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	9454.48**	1690.72	<0.01	8974.77**	1557.36	<0.01	8693.25**	1518.23	<0.01
60	11015.96**	1787.56	<0.01	10225.46**	1668.33	<0.01	10098.02**	1624.52	<0.01
70	10883.06**	1915.21	<0.01	10504.41**	1777.67	<0.01	10276.31**	1740.63	<0.01
80	10537.78**	1995.40	<0.01	11237.67**	1899.62	<0.01	10978.97**	1846.34	<0.01
90	11200.36**	2105.92	<0.01	11890.49**	2013.02	<0.01	12439.52**	1961.65	<0.01
100	10936.07**	2205.37	<0.01	12307.06**	2107.87	<0.01	12791.53**	2035.20	<0.01
110	11797.42**	2295.87	<0.01	10780.67**	2155.14	<0.01	12267.20**	2115.08	<0.01
120	11813.48**	2369.85	<0.01	12251.08**	2258.58	<0.01	13168.53**	2167.89	<0.01
130	12623.30**	2420.80	<0.01	12530.10**	2300.35	<0.01	14473.58**	2210.53	<0.01
140	12701.84**	2512.89	<0.01	13670.05**	2341.76	<0.01	14453.36**	2244.82	<0.01
150	13020.38**	2582.66	<0.01	13764.32**	2378.25	<0.01	14861.68**	2314.48	<0.01
160	14351.77**	2709.63	<0.01	13031.01**	2425.73	<0.01	14964.90**	2374.94	<0.01
170	15324.58**	2719.40	<0.01	14782.75**	2534.68	<0.01	16512.52**	2483.22	<0.01
180	15769.84**	2733.77	<0.01	16083.21**	2581.99	<0.01	17474.82**	2501.27	<0.01
190	17442.76**	2799.66	<0.01	17489.40**	2644.91	<0.01	18828.09**	2531.69	<0.01
200	17517.26**	2819.56	<0.01	18250.27**	2706.50	<0.01	19221.92**	2611.78	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A16. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part A costs summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 60days) or till death;

Table A17. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part B costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	3509.18**	792.78	<0.01	3122.30**	710.60	<0.01	3315.67**	686.04	<0.01
60	3727.27**	833.66	<0.01	4201.18**	744.86	<0.01	3995.64**	726.57	<0.01
70	4571.13**	895.49	<0.01	4451.86**	845.88	<0.01	4629.26**	799.74	<0.01
80	5214.89**	940.57	<0.01	4940.15**	905.88	<0.01	5319.65**	846.67	<0.01
90	5441.25**	985.21	<0.01	5236.19**	956.88	<0.01	5587.61**	898.71	<0.01
100	5748.94**	1030.86	<0.01	5636.09**	983.89	<0.01	6012.95**	975.87	<0.01
110	5763.23**	1080.33	<0.01	5678.22**	1019.67	<0.01	6222.67**	973.56	<0.01
120	5967.09**	1049.84	<0.01	6559.54**	1019.46	<0.01	6372.06**	970.96	<0.01
130	5996.90**	1078.47	<0.01	7033.97**	1049.87	<0.01	6771.21**	988.95	<0.01
140	6334.37**	1172.03	<0.01	7551.32**	1061.65	<0.01	7171.69**	1014.58	<0.01
150	7483.48**	1208.19	<0.01	7898.55**	1137.78	<0.01	7961.43**	1074.65	<0.01
160	8013.86**	1254.57	<0.01	7651.10**	1153.82	<0.01	7759.35**	1100.82	<0.01
170	7804.09**	1245.92	<0.01	7964.07**	1195.39	<0.01	8191.37**	1143.60	<0.01
180	8831.53**	1261.36	<0.01	8369.49**	1215.08	<0.01	8827.21**	1157.13	<0.01
190	9422.74**	1287.30	<0.01	9026.80**	1239.10	<0.01	9574.29**	1167.12	<0.01
200	8747.57**	1307.14	<0.01	9511.04**	1266.65	<0.01	9937.80**	1203.05	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A17. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B costs summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 60days) or till death;

Table A18. Instrumental variables estimates of the effectiveness of depression diagnosis on Part B outpatient costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	33.41	499.89	0.95	-33.49	433.22	0.94	100.88	414.29	0.81
60	-78.13	522.99	0.88	289.84	436.03	0.51	137.02	431.77	0.75
70	313.16	554.98	0.57	206.87	540.72	0.70	255.55	488.34	0.60
80	390.76	587.24	0.51	154.43	582.87	0.79	339.17	515.58	0.51
90	311.58	618.89	0.62	177.48	614.55	0.77	225.51	548.14	0.68
100	198.52	645.41	0.76	83.94	614.48	0.89	219.39	620.40	0.72
110	241.02	674.22	0.72	165.46	636.90	0.80	360.87	577.67	0.53
120	528.73	588.68	0.37	633.45	580.88	0.28	524.32	540.01	0.33
130	546.49	606.28	0.37	928.92	606.89	0.13	596.08	557.33	0.29
140	592.24	720.45	0.41	1157.90*	604.72	0.06	873.19	566.89	0.12
150	1336.75*	721.68	0.06	1362.43**	697.65	0.05	1244.575**	629.46	0.05
160	1468.16**	751.95	0.05	1138.58	707.81	0.11	1008.91	646.07	0.12
170	1337.82*	741.86	0.07	1059.83	727.56	0.15	1170.88*	668.18	0.08
180	1735.202**	749.02	0.02	1243.87*	738.73	0.09	1315.18**	672.50	0.05
190	1638.608**	759.02	0.03	1580.643**	752.23	0.04	1483.202**	668.80	0.03
200	1132.63	778.93	0.15	1773.545**	767.09	0.02	1695.197**	686.93	0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A18. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B outpatient costs summed up all standardized payments from outpatient claims over the 1 year period post (the index date + 60days) or till death;

Table A19. Instrumental variables estimates of the effectiveness of depression diagnosis on Part B physician fee schedule costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	2870.05**	308.01	<0.01	2412.57**	279.10	<0.01	2483.53**	275.64	<0.01
60	3037.58**	325.16	<0.01	3051.56**	302.08	<0.01	3023.88**	295.93	<0.01
70	3157.60**	346.97	<0.01	3282.09**	323.85	<0.01	3322.79**	318.73	<0.01
80	3475.40**	365.19	<0.01	3572.79**	347.73	<0.01	3708.53**	340.28	<0.01
90	3840.20**	386.83	<0.01	3833.73**	370.36	<0.01	4075.31**	360.84	<0.01
100	4033.31**	404.55	<0.01	4099.96**	388.38	<0.01	4275.62**	378.49	<0.01
110	4168.69**	425.79	<0.01	4264.17**	401.99	<0.01	4444.94**	393.43	<0.01
120	4124.11**	442.50	<0.01	4546.02**	421.59	<0.01	4480.83**	403.31	<0.01
130	4284.13**	452.56	<0.01	4645.42**	430.47	<0.01	4788.30**	413.58	<0.01
140	4177.78**	464.95	<0.01	4800.47**	439.06	<0.01	4843.78**	422.66	<0.01
150	4621.42**	484.55	<0.01	4910.71**	449.24	<0.01	5145.76**	439.40	<0.01
160	4948.48**	505.55	<0.01	4890.65**	457.05	<0.01	5223.10**	451.85	<0.01
170	5097.92**	508.07	<0.01	5303.58**	480.97	<0.01	5530.57**	473.94	<0.01
180	5306.51**	513.63	<0.01	5435.24**	487.94	<0.01	5812.91**	478.47	<0.01
190	5794.56**	530.20	<0.01	5829.91**	500.87	<0.01	6268.33**	490.54	<0.01
200	5673.59**	536.08	<0.01	6103.98**	516.36	<0.01	6462.38**	511.76	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A19. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B physician fee schedule costs summed up all standardized payments from standardized carrier and durable medical equipment claims for physician fee schedules over the 1 year period post (the index date + 60days) or till death;

Table A20. Instrumental variables estimates of the effectiveness of depression diagnosis on other Part B costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	605.72**	308.78	<0.01	743.23**	285.20	<0.01	731.27**	272.64	<0.01
60	767.83**	326.72	<0.01	859.78**	304.22	<0.01	834.73**	290.54	<0.01
70	1100.37**	363.74	<0.01	962.91**	331.57	<0.01	1050.92**	318.88	<0.01
80	1348.73**	379.31	<0.01	1212.92**	349.79	<0.01	1271.95**	333.00	<0.01
90	1289.47**	380.43	<0.01	1224.98**	367.19	<0.01	1286.80**	355.50	<0.01
100	1517.11**	402.19	<0.01	1452.19**	390.83	<0.01	1517.94**	386.61	<0.01
110	1353.52**	422.97	<0.01	1248.59**	405.94	<0.01	1416.86**	407.12	<0.01
120	1314.25**	433.45	<0.01	1380.06**	427.85	<0.01	1366.90**	420.05	<0.01
130	1166.28**	448.40	<0.01	1459.63**	435.69	<0.01	1386.83**	420.93	<0.01
140	1564.36**	463.37	<0.01	1592.95**	442.68	<0.01	1454.72**	434.66	<0.01
150	1525.32**	498.43	<0.01	1625.41**	457.65	<0.01	1571.09**	445.38	<0.01
160	1597.23**	500.80	<0.01	1621.87**	463.69	<0.01	1527.34**	452.86	<0.01
170	1368.35**	499.86	<0.01	1600.66**	479.47	<0.01	1489.92**	469.22	<0.01
180	1789.81**	502.21	<0.01	1690.38**	489.10	<0.01	1699.11**	474.93	<0.01
190	1989.57**	511.62	<0.01	1616.25**	490.89	<0.01	1822.76**	481.25	<0.01
200	1941.35**	519.90	<0.01	1633.52**	499.58	<0.01	1780.22**	493.35	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A20. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Other Part B costs summed up all standardized payments from standardized carrier and durable medical equipment claims for non-physician fee schedules, including ambulatory surgery center, durable medical equipment, anesthesia, prosthetics, orthotics, lab, drugs, and ambulance over the 1 year period post (the index date + 60days) or till death;

Table A21. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part D costs for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	359.40	244.51	0.14	357.25*	213.55	0.09	356.35*	210.26	0.09
60	499.138**	254.05	0.05	332.81	226.99	0.14	386.83*	222.87	0.08
70	476.87*	274.55	0.08	319.02	243.53	0.19	362.71	240.99	0.13
80	402.08	270.71	0.14	444.75*	261.26	0.09	513.112**	250.19	0.04
90	315.37	292.70	0.28	312.18	276.18	0.26	428.75	267.34	0.11
100	619.63**	322.17	0.05	468.82*	286.32	0.10	531.53*	280.84	0.06
110	886.917**	330.75	0.01	506.81*	294.27	0.09	569.09**	291.01	0.05
120	753.127**	341.75	0.03	677.339**	312.06	0.03	509.34*	296.63	0.09
130	741.763**	355.08	0.04	684.650**	317.04	0.03	545.94*	304.15	0.07
140	789.568**	366.11	0.03	688.305**	322.49	0.03	572.91*	309.01	0.06
150	634.47*	354.86	0.07	503.26	326.90	0.12	570.62*	318.18	0.07
160	809.333**	366.55	0.03	764.888**	333.27	0.02	682.667**	325.85	0.04
170	986.932**	365.23	0.01	896.191**	345.92	0.01	759.684**	335.71	0.02
180	1038.117**	368.62	0.01	1111.204**	353.94	<0.01	1020.894**	338.60	<0.01
190	1033.688**	401.67	0.01	963.247**	360.21	0.01	861.210**	344.26	0.01
200	1064.600**	403.74	0.01	975.132**	368.37	0.01	1042.900**	354.99	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A21. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part D costs summed up all standardized payments from Part D prescription drug claims over the 1 year period post (the index date + 60days) or till death;

Table A22. Instrumental variables estimates of the effectiveness of depression diagnosis on hospitalizations for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	0.38**	0.12	<0.01	0.25**	0.11	0.02	0.24**	0.11	0.02
60	0.38**	0.12	<0.01	0.29**	0.11	0.01	0.31**	0.11	0.01
70	0.32**	0.13	0.02	0.28**	0.12	0.02	0.27**	0.12	0.02
80	0.27**	0.14	0.05	0.35**	0.13	0.01	0.31**	0.13	0.01
90	0.32**	0.15	0.03	0.34**	0.14	0.02	0.34**	0.13	0.01
100	0.24	0.15	0.12	0.31**	0.14	0.03	0.37**	0.14	0.01
110	0.19	0.16	0.23	0.23	0.15	0.13	0.30**	0.15	0.04
120	0.21	0.16	0.21	0.27*	0.16	0.08	0.31**	0.15	0.04
130	0.26	0.17	0.13	0.32**	0.16	0.04	0.39**	0.15	0.01
140	0.28	0.17	0.11	0.37**	0.16	0.02	0.41**	0.16	0.01
150	0.29*	0.18	0.10	0.37**	0.17	0.02	0.43**	0.16	0.01
160	0.31*	0.19	0.10	0.36**	0.17	0.03	0.44**	0.16	0.01
170	0.34*	0.19	0.07	0.39**	0.18	0.03	0.46**	0.17	0.01
180	0.44**	0.19	0.02	0.50**	0.18	0.01	0.56**	0.17	<0.01
190	0.63**	0.19	<0.01	0.55**	0.18	<0.01	0.63**	0.17	<0.01
200	0.57**	0.19	<0.01	0.64**	0.19	<0.01	0.65**	0.18	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A22. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 60days) or till death;

Table A23. Instrumental variables estimates of the effectiveness of depression diagnosis on ED visits for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.05	0.15	0.77	-0.13	0.14	0.35	-0.16	0.13	0.23
60	-0.06	0.16	0.71	-0.15	0.15	0.29	-0.18	0.14	0.20
70	-0.14	0.17	0.42	-0.10	0.16	0.53	-0.16	0.15	0.29
80	-0.17	0.18	0.33	-0.15	0.17	0.38	-0.19	0.16	0.23
90	-0.20	0.19	0.29	-0.15	0.18	0.39	-0.20	0.17	0.25
100	-0.22	0.19	0.25	-0.22	0.19	0.23	-0.19	0.18	0.29
110	-0.35*	0.20	0.08	-0.43**	0.19	0.03	-0.38**	0.18	0.04
120	-0.36*	0.21	0.09	-0.45**	0.20	0.03	-0.45**	0.19	0.02
130	-0.35	0.22	0.11	-0.32	0.20	0.12	-0.36*	0.19	0.06
140	-0.37*	0.22	0.10	-0.39*	0.21	0.06	-0.39**	0.20	0.05
150	-0.34	0.23	0.14	-0.35*	0.21	0.10	-0.36*	0.20	0.07
160	-0.36	0.24	0.14	-0.43**	0.22	0.05	-0.45**	0.21	0.03
170	-0.40*	0.24	0.10	-0.45**	0.22	0.04	-0.46**	0.22	0.04
180	-0.04	0.24	0.87	-0.26	0.23	0.25	-0.30	0.22	0.17
190	-0.09	0.24	0.71	-0.16	0.23	0.48	-0.28	0.22	0.20
200	-0.17	0.25	0.50	-0.19	0.24	0.41	-0.27	0.23	0.23

Notes:

ED: emergency department;
ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A23. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 60days) or till death;

Table A24. Instrumental variables estimates of the effectiveness of depression diagnosis on outpatient visits for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-1.82**	0.63	<0.01	-2.36**	0.58	<0.01	-2.13**	0.56	<0.01
60	-1.95**	0.66	<0.01	-1.94**	0.61	<0.01	-1.87**	0.60	<0.01
70	-0.67	0.70	0.34	-1.37**	0.66	0.04	-1.42**	0.64	0.03
80	-1.25*	0.74	0.09	-1.81**	0.70	0.01	-1.52**	0.67	0.02
90	-1.56**	0.79	0.05	-0.86	0.74	0.24	-1.41**	0.71	0.05
100	-1.29	0.82	0.12	-1.92**	0.78	0.01	-1.70**	0.74	0.02
110	-0.53	0.85	0.54	-1.21	0.80	0.13	-1.28*	0.77	0.10
120	-0.54	0.88	0.54	-1.42*	0.84	0.09	-1.55**	0.80	0.05
130	-0.77	0.90	0.39	-1.20	0.86	0.16	-1.87**	0.80	0.02
140	-0.50	0.94	0.60	-0.93	0.87	0.29	-1.36*	0.82	0.10
150	-0.51	0.96	0.59	-0.60	0.88	0.49	-1.10	0.84	0.19
160	-0.23	1.00	0.82	-1.31	0.90	0.15	-1.54*	0.87	0.08
170	0.40	1.00	0.69	-1.03	0.94	0.28	-1.04	0.91	0.25
180	1.60	1.01	0.11	-0.42	0.94	0.65	-0.82	0.91	0.37
190	1.37	1.03	0.18	0.01	0.96	0.99	-1.18	0.91	0.20
200	1.00	1.04	0.34	0.83	0.99	0.40	-0.12	0.95	0.90

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A24. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 60days) or till death;

Table A25. Instrumental variables estimates of the effectiveness of depression diagnosis on physician visits for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	14.94**	1.51	<0.01	13.80**	1.38	<0.01	13.78**	1.35	<0.01
60	17.19**	1.61	<0.01	16.06**	1.49	<0.01	16.24**	1.45	<0.01
70	18.69**	1.73	<0.01	17.77**	1.60	<0.01	18.32**	1.56	<0.01
80	19.42**	1.80	<0.01	19.79**	1.71	<0.01	20.03**	1.66	<0.01
90	21.32**	1.92	<0.01	21.30**	1.82	<0.01	21.82**	1.77	<0.01
100	23.01**	2.02	<0.01	22.26**	1.91	<0.01	22.69**	1.85	<0.01
110	22.89**	2.12	<0.01	22.57**	1.98	<0.01	23.64**	1.94	<0.01
120	22.36**	2.18	<0.01	24.06**	2.08	<0.01	23.74**	1.98	<0.01
130	22.92**	2.23	<0.01	25.05**	2.13	<0.01	25.03**	2.04	<0.01
140	23.29**	2.32	<0.01	25.97**	2.18	<0.01	25.65**	2.08	<0.01
150	24.66**	2.39	<0.01	27.13**	2.22	<0.01	27.64**	2.16	<0.01
160	27.06**	2.52	<0.01	26.81**	2.26	<0.01	28.08**	2.22	<0.01
170	27.27**	2.51	<0.01	27.97**	2.36	<0.01	28.88**	2.31	<0.01
180	28.13**	2.54	<0.01	29.50**	2.41	<0.01	30.83**	2.35	<0.01
190	30.73**	2.63	<0.01	31.20**	2.48	<0.01	31.99**	2.39	<0.01
200	30.12**	2.65	<0.01	32.60**	2.55	<0.01	32.88**	2.48	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A25. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Physician visits were based on the number of outpatient/carrier claims for evaluation and management services by physicians over the 1-year period post (the index date + 60days) or till death;

Table A26. Instrumental variables estimates of the effectiveness of depression diagnosis on prescription claims for elderly patients with acute myocardial infarction (60-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-4.87*	2.59	0.06	-4.11*	2.37	0.08	-4.12*	2.31	0.08
60	-6.02**	2.72	0.03	-6.68**	2.53	0.01	-5.25**	2.45	0.03
70	-9.05**	2.92	<0.01	-7.78**	2.71	<0.01	-8.18**	2.63	<0.01
80	-9.72**	3.05	<0.01	-10.83**	2.89	<0.01	-8.83**	2.79	<0.01
90	-8.64**	3.21	<0.01	-12.45**	3.05	<0.01	-10.65**	2.95	<0.01
100	-8.74**	3.36	<0.01	-10.96**	3.17	<0.01	-10.13**	3.05	<0.01
110	-9.98**	3.52	<0.01	-10.96**	3.29	<0.01	-10.91**	3.19	<0.01
120	-12.72**	3.64	<0.01	-10.89**	3.45	<0.01	-13.16**	3.30	<0.01
130	-13.99**	3.74	<0.01	-12.74**	3.54	<0.01	-13.57**	3.37	<0.01
140	-13.28**	3.87	<0.01	-12.65**	3.59	<0.01	-13.11**	3.44	<0.01
150	-13.68**	3.97	<0.01	-12.61**	3.65	<0.01	-12.60**	3.53	<0.01
160	-12.96**	4.14	<0.01	-12.73**	3.72	<0.01	-13.05**	3.63	<0.01
170	-15.32**	4.13	<0.01	-14.67**	3.88	<0.01	-13.52**	3.77	<0.01
180	-15.39**	4.16	<0.01	-14.38**	3.93	<0.01	-11.80**	3.80	<0.01
190	-19.26**	4.26	<0.01	-17.89**	4.01	<0.01	-14.86**	3.85	<0.01
200	-18.60**	4.31	<0.01	-18.83**	4.10	<0.01	-15.07**	3.95	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A26. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 60days) or till death;

Table A27. Instrumental variables estimates of the effectiveness of depression diagnosis on survival for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.05*	0.03	0.09	-0.05**	0.03	0.05	-0.06**	0.02	0.01
60	-0.04	0.03	0.18	-0.05*	0.03	0.07	-0.05*	0.03	0.08
70	-0.04	0.03	0.18	-0.06**	0.03	0.03	-0.06**	0.03	0.04
80	-0.05	0.03	0.12	-0.04	0.03	0.17	-0.05*	0.03	0.07
90	-0.05	0.03	0.13	-0.05	0.03	0.12	-0.05	0.03	0.11
100	-0.06*	0.03	0.10	-0.04	0.03	0.18	-0.04	0.03	0.23
110	-0.04	0.04	0.25	-0.05	0.03	0.12	-0.04	0.03	0.25
120	-0.04	0.04	0.31	-0.04	0.03	0.23	-0.04	0.03	0.18
130	-0.05	0.04	0.16	-0.04	0.04	0.30	-0.04	0.03	0.28
140	-0.04	0.04	0.36	-0.03	0.04	0.46	-0.03	0.04	0.35
150	-0.02	0.04	0.56	-0.03	0.04	0.39	-0.04	0.04	0.32
160	-0.01	0.04	0.86	-0.02	0.04	0.65	-0.02	0.04	0.62
170	0.00	0.04	0.93	-0.02	0.04	0.65	-0.02	0.04	0.67
180	-0.01	0.04	0.81	-0.01	0.04	0.84	-0.01	0.04	0.78
190	0.00	0.04	0.93	0.00	0.04	0.99	-0.01	0.04	0.84
200	0.01	0.04	0.82	0.00	0.04	0.92	-0.01	0.04	0.80

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A27. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Survival was set to 1 if a patient survived the first year after the index AMI admission, 0 otherwise.

Table A28. Instrumental variables estimates of the effectiveness of depression diagnosis on total healthcare costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	9190.50**	1868.21	<0.01	11151.35**	1762.14	<0.01	10400.08**	1691.60	<0.01
60	12221.35**	1975.47	<0.01	12750.06**	1853.08	<0.01	12768.98**	1813.29	<0.01
70	13539.71**	2070.56	<0.01	12757.84**	1967.54	<0.01	13466.03**	1896.76	<0.01
80	14739.01**	2217.79	<0.01	14830.43**	2104.31	<0.01	15342.99**	2039.30	<0.01
90	16414.30**	2311.26	<0.01	16656.41**	2176.06	<0.01	16626.74**	2131.42	<0.01
100	15082.59**	2422.34	<0.01	16711.52**	2252.48	<0.01	16636.75**	2201.59	<0.01
110	17572.05**	2529.71	<0.01	16628.28**	2330.79	<0.01	17120.11**	2261.84	<0.01
120	16793.16**	2535.08	<0.01	16856.93**	2425.30	<0.01	18133.80**	2337.55	<0.01
130	19663.53**	2711.65	<0.01	19514.66**	2485.60	<0.01	20101.28**	2397.18	<0.01
140	18905.68**	2758.25	<0.01	19838.98**	2591.80	<0.01	20419.02**	2486.14	<0.01
150	19170.80**	2786.07	<0.01	21366.37**	2664.35	<0.01	21273.33**	2555.04	<0.01
160	20589.46**	2874.05	<0.01	23019.89**	2731.98	<0.01	22164.71**	2631.79	<0.01
170	23824.18**	3005.38	<0.01	24858.33**	2793.62	<0.01	24882.05**	2692.96	<0.01
180	25163.78**	3066.53	<0.01	24646.28**	2825.80	<0.01	25584.90**	2723.50	<0.01
190	25825.13**	3181.16	<0.01	25888.46**	2867.30	<0.01	27136.40**	2805.31	<0.01
200	24837.92**	3197.24	<0.01	25463.95**	2970.25	<0.01	26526.79**	2868.28	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A28. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 90days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Table A29. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part A costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	6589.78**	1462.97	<0.01	7510.73**	1373.80	<0.01	7381.21**	1325.72	<0.01
60	8389.64**	1544.68	<0.01	8606.46**	1446.44	<0.01	8734.47**	1422.49	<0.01
70	8929.59**	1616.12	<0.01	8483.32**	1533.59	<0.01	9125.47**	1484.41	<0.01
80	9671.62**	1734.98	<0.01	9446.53**	1639.58	<0.01	10011.12**	1596.73	<0.01
90	11045.79**	1806.53	<0.01	11005.72**	1702.77	<0.01	11190.13**	1669.37	<0.01
100	9573.18**	1893.64	<0.01	10990.26**	1766.10	<0.01	10943.06**	1724.89	<0.01
110	11625.85**	1975.48	<0.01	10806.28**	1823.84	<0.01	11086.31**	1768.82	<0.01
120	10514.24**	1981.38	<0.01	10818.27**	1897.50	<0.01	11932.66**	1825.93	<0.01
130	12528.98**	2117.21	<0.01	12755.84**	1941.31	<0.01	13268.91**	1871.56	<0.01
140	11915.19**	2141.50	<0.01	13129.68**	2003.64	<0.01	13402.37**	1933.36	<0.01
150	12293.76**	2168.52	<0.01	13794.72**	2054.71	<0.01	13778.39**	1983.24	<0.01
160	13277.34**	2232.11	<0.01	14889.05**	2121.81	<0.01	14376.16**	2043.91	<0.01
170	15679.17**	2332.69	<0.01	16276.65**	2168.20	<0.01	16495.79**	2087.58	<0.01
180	16306.53**	2375.01	<0.01	16064.60**	2178.74	<0.01	16878.27**	2105.09	<0.01
190	16671.97**	2466.30	<0.01	17075.10**	2226.37	<0.01	18059.02**	2173.98	<0.01
200	16223.43**	2481.42	<0.01	16774.14**	2292.00	<0.01	17667.78**	2199.22	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A29. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part A costs summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 90days) or till death;

Table A30. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part B costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	2134.68**	666.26	<0.01	3503.71**	666.70	<0.01	2603.69**	596.14	<0.01
60	3296.54**	707.34	<0.01	3753.37**	709.03	<0.01	3487.76**	637.14	<0.01
70	3914.56**	740.54	<0.01	4840.59**	756.08	<0.01	3902.86**	672.74	<0.01
80	4373.15**	781.35	<0.01	5077.42**	760.87	<0.01	4731.06**	715.18	<0.01
90	4662.78**	816.15	<0.01	5147.66**	783.04	<0.01	4865.75**	741.41	<0.01
100	4746.85**	854.09	<0.01	5199.57**	815.78	<0.01	5040.54**	766.66	<0.01
110	5285.57**	892.32	<0.01	5502.41**	845.47	<0.01	5378.00**	787.37	<0.01
120	5662.46**	885.52	<0.01	6118.55**	867.72	<0.01	5540.24**	812.60	<0.01
130	6391.10**	947.65	<0.01	6055.09**	958.65	<0.01	6099.51**	834.81	<0.01
140	6229.03**	995.25	<0.01	6850.00**	986.31	<0.01	6348.91**	883.06	<0.01
150	6055.92**	999.73	<0.01	7332.64**	963.50	<0.01	6702.50**	916.14	<0.01
160	6601.94**	1036.95	<0.01	7684.90**	980.35	<0.01	6904.10**	932.87	<0.01
170	7329.45**	1077.67	<0.01	7746.40**	1035.27	<0.01	7473.21**	951.22	<0.01
180	8021.56**	1096.81	<0.01	7832.38**	1003.19	<0.01	7885.06**	980.02	<0.01
190	8116.40**	1132.39	<0.01	7816.59**	1084.67	<0.01	8131.42**	985.95	<0.01
200	7593.34**	1133.96	<0.01	16774.14**	2292.00	<0.01	8081.96**	1074.86	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A30. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B costs summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 90days) or till death;

Table A31. Instrumental variables estimates of the effectiveness of depression diagnosis on Part B outpatient costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-49.77	398.54	0.90	70.87	387.93	0.86	-133.43	351.80	0.70
60	102.88	421.55	0.81	153.70	404.20	0.70	129.67	376.12	0.73
70	319.77	437.73	0.47	220.73	426.70	0.61	253.36	391.47	0.52
80	401.03	464.33	0.39	647.58	455.90	0.16	493.43	415.72	0.24
90	126.64	482.64	0.79	670.04	435.96	0.12	565.70	422.59	0.18
100	169.85	504.51	0.74	489.99	449.16	0.28	461.42	434.02	0.29
110	371.16	522.38	0.48	439.28	462.73	0.34	576.53	443.71	0.19
120	979.72**	498.93	0.05	578.32	479.26	0.23	589.81	455.30	0.20
130	1147.29**	541.07	0.03	792.07	492.60	0.11	868.82*	468.14	0.06
140	1375.26**	615.11	0.03	958.70	596.81	0.11	925.48*	518.21	0.07
150	1086.57*	612.43	0.08	1287.62**	612.14	0.04	1011.07*	542.09	0.06
160	1246.52**	633.55	0.05	1270.58**	542.60	0.02	1076.12**	533.83	0.04
170	1487.04**	656.36	0.02	1247.43**	552.16	0.02	1096.01**	536.53	0.04
180	1270.91**	659.24	0.05	1349.73**	642.73	0.04	1240.44**	573.04	0.03
190	1556.82**	683.98	0.02	1367.35**	566.06	0.02	1379.54**	556.10	0.01
200	1454.29**	685.02	0.03	1620.74**	672.55	0.02	1454.61**	691.70	0.04

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A31. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B outpatient costs summed up all standardized payments from outpatient claims over the 1 year period post (the index date + 90days) or till death;

Table A32. Instrumental variables estimates of the effectiveness of depression diagnosis on Part B physician fee schedule costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	1758.66**	266.69	<0.01	2261.14**	252.23	<0.01	2130.30**	243.60	<0.01
60	2293.42**	278.70	<0.01	2504.49**	263.67	<0.01	2534.35**	258.63	<0.01
70	2431.01**	292.17	<0.01	2498.40**	279.43	<0.01	2667.94**	271.28	<0.01
80	2775.93**	313.62	<0.01	2924.78**	300.19	<0.01	3007.46**	289.93	<0.01
90	3083.78**	329.89	<0.01	3074.32**	311.23	<0.01	3100.27**	305.88	<0.01
100	3134.43**	348.50	<0.01	3265.55**	325.29	<0.01	3261.09**	318.79	<0.01
110	3440.69**	366.31	<0.01	3339.24**	336.72	<0.01	3492.06**	327.88	<0.01
120	3248.95**	365.70	<0.01	3429.18**	350.22	<0.01	3563.27**	338.53	<0.01
130	3429.97**	389.99	<0.01	3651.15**	359.64	<0.01	3717.52**	347.74	<0.01
140	3272.60**	391.03	<0.01	3612.26**	372.59	<0.01	3949.09**	362.77	<0.01
150	3446.52**	396.13	<0.01	3923.13**	386.15	<0.01	4174.02**	375.20	<0.01
160	3757.48**	408.89	<0.01	4214.10**	399.05	<0.01	4338.10**	387.24	<0.01
170	4117.98**	428.47	<0.01	4556.24**	409.08	<0.01	4686.60**	396.31	<0.01
180	4834.50**	447.78	<0.01	4724.41**	413.03	<0.01	4964.73**	403.22	<0.01
190	4841.42**	460.64	<0.01	4894.60**	422.22	<0.01	5123.63**	416.65	<0.01
200	4523.72**	458.91	<0.01	4615.99**	431.69	<0.01	5062.31**	420.54	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A32. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part B physician fee schedule costs summed up all standardized payments from standardized carrier and durable medical equipment claims for physician fee schedules over the 1 year period post (the index date + 90days) or till death;

Table A33. Instrumental variables estimates of the effectiveness of depression diagnosis on other Part B costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	425.79	273.54	0.12	778.85**	256.10	<0.01	606.82*	243.39	0.01
60	900.24**	297.82	<0.01	845.53**	272.38	<0.01	823.73**	260.95	<0.01
70	1163.78**	312.90	<0.01	1034.24**	291.66	<0.01	981.57**	283.63	<0.01
80	1196.20**	315.11	<0.01	1268.23**	303.52	<0.01	1230.17**	295.42	<0.01
90	1452.36**	331.03	<0.01	1333.06**	315.04	<0.01	1199.78**	308.17	<0.01
100	1442.57**	345.17	<0.01	1392.11**	322.86	<0.01	1318.02**	322.89	<0.01
110	1473.72**	363.99	<0.01	1421.05**	343.06	<0.01	1309.41**	331.81	<0.01
120	1433.78**	368.18	<0.01	1494.90**	353.48	<0.01	1387.16**	343.85	<0.01
130	1813.84**	390.07	<0.01	1675.34**	360.94	<0.01	1513.16**	356.30	<0.01
140	1581.17**	389.19	<0.01	1484.13**	385.12	<0.01	1474.33**	363.44	<0.01
150	1522.83**	397.73	<0.01	1639.25**	394.42	<0.01	1517.41**	374.88	<0.01
160	1597.94**	414.13	<0.01	1847.96**	405.83	<0.01	1489.88**	389.95	<0.01
170	1724.43**	428.24	<0.01	1881.22**	410.75	<0.01	1690.60**	400.82	<0.01
180	1916.15**	433.87	<0.01	1672.26**	407.61	<0.01	1679.89**	407.42	<0.01
190	1718.16**	445.17	<0.01	1570.43**	418.63	<0.01	1628.25**	414.45	<0.01
200	1615.33**	447.37	<0.01	1579.86**	427.76	<0.01	1565.04**	415.27	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A33. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Other Part B costs summed up all standardized payments from standardized carrier and durable medical equipment claims for non-physician fee schedules, including ambulatory surgery center, durable medical equipment, anesthesia, prosthetics, orthotics, lab, drugs, and ambulance over the 1 year period post (the index date + 90days) or till death;

Table A34. Instrumental variables estimates of the effectiveness of depression diagnosis on Medicare Part D costs for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	466.05**	200.81	0.02	529.76**	194.31	0.01	415.18**	182.55	0.02
60	535.18**	210.42	0.01	639.89**	203.70	<0.01	546.76**	194.97	0.01
70	695.56**	222.19	<0.01	521.14**	211.57	0.01	437.69**	204.98	0.03
80	694.24**	235.93	<0.01	543.32**	226.13	0.02	600.81**	219.25	0.01
90	705.72**	250.59	0.01	573.27**	235.61	0.02	570.86**	231.70	0.01
100	762.56**	264.27	<0.01	573.60**	239.91	0.02	653.15**	238.28	0.01
110	660.63**	273.59	0.02	622.44**	250.21	0.01	655.80**	246.25	0.01
120	616.46**	277.43	0.03	536.25**	269.04	0.05	660.90**	256.96	0.01
130	743.46**	291.92	0.01	640.27**	270.51	0.02	732.86**	265.01	0.01
140	761.46**	296.19	0.01	654.21**	277.67	0.02	667.74**	269.65	0.01
150	821.12**	295.83	0.01	721.66**	285.80	0.01	792.44**	277.77	<0.01
160	710.18**	308.38	0.02	798.20**	292.95	0.01	884.46**	281.30	<0.01
170	815.56**	320.82	0.01	896.79**	297.21	<0.01	913.06**	286.66	<0.01
180	835.69**	327.51	0.01	835.29**	301.32	0.01	821.58**	290.26	0.01
190	1036.77**	336.72	<0.01	980.98**	307.82	<0.01	945.96**	295.75	<0.01
200	1021.15**	356.91	<0.01	873.22**	316.78	0.01	777.06**	297.35	0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A34. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Part D costs summed up all standardized payments from Part D prescription drug claims over the 1 year period post (the index date + 90days) or till death;

Table A35. Instrumental variables estimates of the effectiveness of depression diagnosis on hospitalizations for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	0.10	0.10	0.33	0.18*	0.10	0.06	0.16*	0.09	0.08
60	0.24**	0.11	0.03	0.23**	0.10	0.02	0.23**	0.10	0.02
70	0.21*	0.11	0.06	0.17	0.11	0.12	0.20**	0.10	0.05
80	0.27**	0.12	0.03	0.24**	0.11	0.04	0.25**	0.11	0.02
90	0.35***	0.13	0.01	0.32**	0.12	0.01	0.30**	0.12	0.01
100	0.20	0.13	0.13	0.32**	0.12	0.01	0.29**	0.12	0.02
110	0.30**	0.14	0.03	0.28**	0.13	0.03	0.29**	0.12	0.02
120	0.29**	0.14	0.04	0.26**	0.13	0.05	0.33**	0.13	0.01
130	0.31**	0.15	0.03	0.37**	0.14	0.01	0.39**	0.13	<0.01
140	0.28*	0.15	0.06	0.31**	0.14	0.03	0.35**	0.13	0.01
150	0.34**	0.15	0.02	0.33**	0.14	0.02	0.38**	0.14	0.01
160	0.36**	0.16	0.02	0.46**	0.15	<0.01	0.44**	0.14	<0.01
170	0.47**	0.16	<0.01	0.53**	0.15	<0.01	0.54**	0.14	<0.01
180	0.56**	0.16	<0.01	0.53**	0.15	<0.01	0.57**	0.14	<0.01
190	0.54**	0.17	<0.01	0.52**	0.15	<0.01	0.59**	0.15	<0.01
200	0.54**	0.17	<0.01	0.53**	0.16	<0.01	0.56**	0.15	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A35. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 90days) or till death;

Table A36. Instrumental variables estimates of the effectiveness of depression diagnosis on ED visits for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.21*	0.13	0.10	-0.16	0.13	0.19	-0.23*	0.12	0.06
60	-0.08	0.14	0.56	-0.15	0.13	0.25	-0.18	0.13	0.15
70	-0.08	0.15	0.59	-0.18	0.14	0.21	-0.18	0.13	0.18
80	-0.04	0.16	0.78	-0.12	0.15	0.41	-0.16	0.14	0.27
90	0.03	0.16	0.87	0.00	0.15	0.98	-0.08	0.15	0.61
100	-0.23	0.17	0.17	-0.10	0.16	0.53	-0.19	0.15	0.22
110	-0.19	0.18	0.27	-0.26	0.16	0.11	-0.27	0.16	0.09
120	-0.14	0.18	0.43	-0.25	0.17	0.14	-0.22	0.17	0.17
130	-0.06	0.19	0.75	-0.15	0.18	0.39	-0.21	0.17	0.21
140	-0.12	0.19	0.55	-0.23	0.18	0.21	-0.25	0.17	0.15
150	-0.15	0.19	0.43	-0.20	0.19	0.29	-0.27	0.18	0.12
160	-0.06	0.20	0.75	-0.07	0.19	0.72	-0.22	0.18	0.22
170	0.00	0.21	0.99	-0.02	0.19	0.93	-0.10	0.18	0.57
180	0.16	0.21	0.46	-0.02	0.19	0.90	-0.09	0.19	0.64
190	-0.01	0.22	0.95	-0.09	0.20	0.64	-0.10	0.19	0.60
200	0.04	0.22	0.86	-0.07	0.20	0.71	-0.13	0.20	0.52

Notes:

ED: emergency department;
ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A36. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 90days) or till death;

Table A37. Instrumental variables estimates of the effectiveness of depression diagnosis on outpatient visits for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.55	0.54	0.31	-0.58	0.51	0.25	-0.63	0.49	0.19
60	0.06	0.58	0.92	-0.35	0.54	0.51	-0.45	0.52	0.39
70	0.47	0.59	0.43	0.08	0.57	0.88	-0.18	0.55	0.75
80	0.65	0.64	0.31	0.49	0.61	0.42	0.08	0.58	0.89
90	0.15	0.67	0.83	0.52	0.63	0.41	0.53	0.61	0.38
100	0.06	0.70	0.93	0.28	0.65	0.66	0.07	0.62	0.92
110	0.98	0.74	0.19	0.62	0.67	0.35	0.65	0.64	0.31
120	1.36*	0.74	0.07	0.18	0.70	0.79	0.38	0.67	0.57
130	1.65**	0.78	0.04	0.35	0.72	0.63	0.48	0.68	0.48
140	1.74**	0.80	0.03	0.34	0.75	0.65	0.21	0.71	0.76
150	1.60**	0.81	0.05	0.99	0.76	0.19	0.44	0.73	0.55
160	1.94**	0.83	0.02	1.75**	0.78	0.03	0.66	0.75	0.38
170	3.29**	0.87	<0.01	2.41**	0.79	<0.01	1.32*	0.76	0.09
180	2.65**	0.88	<0.01	1.50*	0.79	0.06	1.01	0.77	0.19
190	3.19**	0.91	<0.01	1.86**	0.82	0.02	1.67**	0.80	0.04
200	4.01**	0.92	<0.01	2.63**	0.85	<0.01	1.87**	0.81	0.02

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A37. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 90days) or till death;

Table A38. Instrumental variables estimates of the effectiveness of depression diagnosis on physician visits for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	10.85**	1.29	<0.01	12.66**	1.22	<0.01	12.24**	1.16	<0.01
60	13.49**	1.37	<0.01	13.98**	1.29	<0.01	14.23**	1.25	<0.01
70	14.39**	1.44	<0.01	14.35**	1.36	<0.01	14.87**	1.31	<0.01
80	16.33**	1.54	<0.01	16.43**	1.46	<0.01	16.94**	1.41	<0.01
90	18.50**	1.63	<0.01	17.33**	1.52	<0.01	17.92**	1.49	<0.01
100	16.95**	1.70	<0.01	18.24**	1.59	<0.01	18.07**	1.54	<0.01
110	19.10**	1.78	<0.01	18.60**	1.64	<0.01	19.13**	1.60	<0.01
120	18.29**	1.79	<0.01	18.95**	1.72	<0.01	19.54**	1.65	<0.01
130	19.93**	1.92	<0.01	20.32**	1.76	<0.01	20.75**	1.69	<0.01
140	20.20**	1.94	<0.01	21.19**	1.83	<0.01	22.14**	1.77	<0.01
150	21.36**	1.98	<0.01	21.64**	1.88	<0.01	23.12**	1.82	<0.01
160	22.14**	2.04	<0.01	23.34**	1.95	<0.01	23.33**	1.87	<0.01
170	24.25**	2.14	<0.01	24.80**	2.00	<0.01	24.89**	1.92	<0.01
180	26.84**	2.21	<0.01	25.21**	2.01	<0.01	26.04**	1.94	<0.01
190	26.25**	2.28	<0.01	25.86**	2.05	<0.01	26.70**	2.01	<0.01
200	25.38**	2.28	<0.01	25.24**	2.11	<0.01	26.52**	2.03	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A38. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Physician visits were based on the number of outpatient/carrier claims for evaluation and management services by physicians over the 1-year period post (the index date + 90days) or till death;

Table A39. Instrumental variables estimates of the effectiveness of depression diagnosis on prescription claims for elderly patients with acute myocardial infarction (90-day observation window)

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-2.47	2.22	0.27	-2.49	2.08	0.23	-2.17	1.99	0.28
60	-2.94	2.34	0.21	-3.02	2.20	0.17	-2.22	2.13	0.30
70	-3.35	2.45	0.17	-4.20*	2.32	0.07	-4.20*	2.23	0.06
80	-4.90*	2.62	0.06	-6.746**	2.47	0.01	-5.040**	2.38	0.03
90	-3.74	2.73	0.17	-4.60*	2.56	0.07	-4.75*	2.49	0.06
100	-5.43*	2.86	0.06	-4.13	2.64	0.12	-4.56*	2.56	0.08
110	-4.88*	2.97	0.10	-6.22**	2.75	0.02	-5.15**	2.65	0.05
120	-6.97**	3.02	0.02	-7.23**	2.88	0.01	-6.94**	2.74	0.01
130	-6.93**	3.21	0.03	-7.87**	2.93	0.01	-6.89**	2.81	0.01
140	-7.86**	3.25	0.02	-9.46**	3.05	<0.01	-7.81**	2.91	0.01
150	-8.07**	3.28	0.01	-8.30**	3.12	0.01	-7.19**	3.00	0.02
160	-9.37**	3.39	0.01	-8.69**	3.21	0.01	-7.25**	3.08	0.02
170	-8.80**	3.50	0.01	-8.13**	3.25	0.01	-7.24**	3.14	0.02
180	-12.28**	3.58	<0.01	-9.60**	3.26	<0.01	-8.64**	3.15	0.01
190	-13.79**	3.70	<0.01	-10.52**	3.35	<0.01	-9.64**	3.25	<0.01
200	-13.28**	3.72	<0.01	-11.00**	3.42	<0.01	-10.91**	3.29	<0.01

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A39. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 90days) or till death;

Table A40. Instrumental variables estimates of the effectiveness of depression diagnosis on survival for elderly patients with acute myocardial infarction (30-day observation window) using two-stage residual inclusion model

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.06	0.04	0.15	-0.06	0.04	0.12	-0.07*	0.04	0.08
60	-0.06	0.05	0.16	-0.08*	0.04	0.06	-0.06	0.04	0.12
70	-0.08	0.05	0.11	-0.07	0.05	0.11	-0.06	0.04	0.13
80	-0.10*	0.05	0.06	-0.10**	0.05	0.04	-0.09*	0.05	0.07
90	-0.09*	0.06	0.10	-0.08*	0.05	0.10	-0.07	0.05	0.15
100	-0.06	0.06	0.28	-0.07	0.05	0.18	-0.05	0.05	0.29
110	-0.05	0.06	0.36	-0.05	0.05	0.36	-0.04	0.05	0.45
120	-0.03	0.06	0.54	-0.03	0.05	0.58	-0.03	0.05	0.58
130	-0.04	0.06	0.47	-0.02	0.05	0.75	-0.03	0.05	0.61
140	-0.06	0.06	0.37	-0.01	0.05	0.88	-0.03	0.05	0.61
150	-0.03	0.06	0.58	0.01	0.05	0.90	0.00	0.05	0.96
160	-0.05	0.06	0.46	-0.03	0.06	0.62	-0.03	0.06	0.64
170	-0.02	0.06	0.76	-0.02	0.06	0.73	-0.01	0.05	0.82
180	-0.02	0.06	0.70	-0.02	0.06	0.78	-0.01	0.06	0.85
190	-0.04	0.07	0.58	-0.01	0.06	0.84	-0.01	0.06	0.92
200	-0.03	0.07	0.69	0.00	0.06	1.00	-0.01	0.06	0.88

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A40. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Survival was set to 1 if a patient survived the first year after the index AMI admission, 0 otherwise.

Table A41. Instrumental variables estimates of the effectiveness of depression diagnosis on survival for elderly patients with acute myocardial infarction (60-day observation window) using two-stage residual inclusion model

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.06	0.04	0.11	-0.09**	0.04	0.01	-0.09**	0.03	0.01
60	-0.08**	0.04	0.05	-0.07**	0.04	0.05	-0.07*	0.04	0.06
70	-0.08*	0.04	0.06	-0.10**	0.04	0.02	-0.08**	0.04	0.03
80	-0.10**	0.05	0.03	-0.10**	0.04	0.03	-0.09**	0.04	0.04
90	-0.08*	0.05	0.09	-0.08*	0.05	0.07	-0.08*	0.04	0.06
100	-0.06	0.05	0.20	-0.10**	0.05	0.04	-0.08*	0.04	0.09
110	-0.08	0.05	0.12	-0.09*	0.05	0.07	-0.08*	0.05	0.10
120	-0.06	0.05	0.21	-0.07	0.05	0.15	-0.09*	0.05	0.08
130	-0.07	0.05	0.17	-0.07	0.05	0.15	-0.09*	0.05	0.07
140	-0.08	0.06	0.14	-0.05	0.05	0.34	-0.08	0.05	0.12
150	-0.08	0.06	0.18	-0.07	0.05	0.19	-0.07	0.05	0.15
160	-0.06	0.06	0.29	-0.07	0.05	0.17	-0.07	0.05	0.17
170	-0.07	0.06	0.24	-0.06	0.05	0.25	-0.06	0.05	0.29
180	-0.04	0.05	0.50	-0.04	0.05	0.45	-0.04	0.05	0.40
190	-0.07	0.06	0.25	-0.06	0.06	0.29	-0.07	0.05	0.20
200	-0.08	0.06	0.21	-0.03	0.05	0.57	-0.04	0.05	0.40

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A41. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Survival was set to 1 if a patient survived the first year after the index AMI admission, 0 otherwise.

Table A42. Instrumental variables estimates of the effectiveness of depression diagnosis on survival for elderly patients with acute myocardial infarction (90-day observation window) using two-stage residual inclusion model

	ADR tertile groups			ADR quintile groups			ADR decile groups		
Area size	Estimate	Standard Error	p value	Estimate	Standard Error	p value	Estimate	Standard Error	p value
50	-0.04	0.03	0.20	-0.04	0.03	0.14	-0.06**	0.03	0.05
60	-0.03	0.03	0.36	-0.04	0.03	0.19	-0.04	0.03	0.20
70	-0.03	0.03	0.36	-0.06*	0.03	0.09	-0.05	0.03	0.13
80	-0.04	0.04	0.29	-0.03	0.03	0.38	-0.04	0.03	0.21
90	-0.04	0.04	0.29	-0.04	0.04	0.26	-0.04	0.03	0.25
100	-0.05	0.04	0.24	-0.03	0.04	0.36	-0.03	0.03	0.44
110	-0.03	0.04	0.46	-0.04	0.04	0.28	-0.02	0.03	0.48
120	-0.02	0.04	0.57	-0.03	0.04	0.43	-0.03	0.04	0.38
130	-0.05	0.05	0.28	-0.02	0.04	0.52	-0.03	0.04	0.48
140	-0.03	0.04	0.49	-0.02	0.04	0.69	-0.02	0.04	0.52
150	-0.01	0.04	0.73	-0.02	0.04	0.59	-0.03	0.04	0.50
160	0.00	0.04	0.96	-0.01	0.04	0.84	-0.01	0.04	0.80
170	0.01	0.04	0.77	-0.01	0.04	0.84	-0.01	0.04	0.88
180	-0.01	0.04	0.90	0.00	0.04	1.00	0.00	0.04	0.95
190	0.01	0.04	0.82	0.01	0.04	0.80	0.00	0.04	0.99
200	0.02	0.04	0.71	0.01	0.04	0.78	0.00	0.04	0.95

Notes:

ADR: area diagnosis ratio;
Tertile groups: patients were grouped into 3 groups based on their ADR values on ZIP code level;
Quintile groups: patients were grouped into 5 groups based on their ADR values on ZIP code level;
Decile groups: patients were grouped into 10 groups based on their ADR values on ZIP code level;

Table A42. Continued

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
**significant at 95% CI; *significant at 90% CI;
Survival was set to 1 if a patient survived the first year after the index AMI admission, 0 otherwise.

Table A43. Instrumental variables estimates of the effectiveness of depression diagnosis among elderly patients with acute myocardial infarction (Area diagnosis ratios, a sample without prior diagnosis of bipolar disorder, psychotherapy, and antidepressant use, 150-person area, quintile)

30-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.01	0.08	0.93	155.56	0.09*
Total healthcare cost	25042.34**	6347.78	<0.01		0.02**
Part A	14604.34**	4961.20	<0.01		0.06*
Part B	9468.58**	2176.90	<0.01		0.03**
Outpatient	552.51	1262.78	0.66		0.07*
Physician fee schedule	7942.95**	956.85	<0.01		0.47
Others	973.12	815.91	0.23		0.02**
Part D	969.41	641.69	0.13		0.21
Healthcare utilization					
# of hospitalizations	0.18	0.34	0.60		0.55
# of ED visits	-0.88**	0.42	0.04		0.58
# of outpatient visits	-0.27	1.78	0.88		0.05**
# of physician visits	44.99**	4.86	<0.01		0.09
# of prescription claims	-16.92**	7.17	0.02		0.05**

Table A43. Continued

60-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.09	0.06	0.18	167.74	0.62
Total healthcare cost	27738.53**	4753.24	<0.01		0.31
Part A	16669.10**	3639.12	<0.01		0.25
Part B	10623.25**	1808.65	<0.01		0.84
Outpatient	1871.18*	1146.01	0.10		0.97
Physician fee schedule	6450.63**	710.94	<0.01		0.62
Others	2301.44**	693.64	<0.01		0.35
Part D	446.18	478.60	0.35		0.06*
Healthcare utilization					
# of hospitalizations	0.39	0.25	0.12		0.35
# of ED visits	-0.48	0.32	0.14		0.01**
# of outpatient visits	-0.35	1.34	0.79		0.01**
# of physician visits	35.77**	3.47	<0.01		0.84
# of prescription claims	-16.64**	5.35	<0.01		0.35

Table A43. Continued

90-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.04	0.06	0.51	168.61	0.96
Total healthcare cost	25607.13**	4022.76	<0.01		0.96
Part A	16169.32**	3081.96	<0.01		0.91
Part B	8625.31**	1530.06	<0.01		0.54
Outpatient	1559.52	981.85	0.11		0.22
Physician fee schedule	4929.25**	592.90	<0.01		0.95
Others	2136.54**	590.87	<0.01		0.62
Part D	812.51**	414.28	0.05		0.84
Healthcare utilization					
# of hospitalizations	0.35	0.22	0.11		0.83
# of ED visits	-0.22	0.28	0.42		0.92
# of outpatient visits	1.43	1.14	0.21		<0.01**
# of physician visits	27.35**	2.87	<0.01		0.55
# of prescription claims	-9.38**	4.49	0.04		0.15

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
ED (emergency department);
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Table A43. Continued

Notes:
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.
**significant at 95% CI; *significant at 90% CI;
Chow F-tests examined whether the instruments described a statistically significant portion of variation in depression diagnosis. A "rule of thumb" for a strong instrument relationship is a Chow F-value > 10.[213]
Hansen over-identification tests were used to examine whether excluding the area diagnosis ratio (ADR)-based instruments from the second stage of 2SLS was appropriate (null hypothesis)[214]

Table A44. Instrumental variables estimates of the effectiveness of depression diagnosis among elderly patients with acute myocardial infarction (Area diagnosis ratios by excluding a patient from the calculation of that patient's area diagnosis ratios, 150-person area, quintile)

30-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.07	0.20	0.72	17.57	0.17
Total healthcare cost	58551.70**	16350.78	<0.01		<0.01**
Part A	33462.12**	12293.75	0.01		0.03**
Part B	22919.00**	5853.50	<0.01		<0.01**
Outpatient	-774.56	3182.58	0.81		0.02**
Physician fee schedule	21441.69**	3289.53	<0.01		0.11
Others	2251.87	2001.15	0.26		0.02**
Part D	2170.59	1567.59	0.17		0.20
Healthcare utilization					
# of hospitalizations	0.62	0.80	0.44		0.58
# of ED visits	-2.27**	1.05	0.03		0.74
# of outpatient visits	-5.41	4.33	0.21		0.11
# of physician visits	110.97**	16.80	<0.01		0.01**
# of prescription claims	-56.51**	19.10	<0.01		0.18

Table A44. Continued

60-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.13	0.15	0.36	22.51	0.53
Total healthcare cost	60328.03**	12226.16	<0.01		0.15
Part A	35087.79**	8922.29	<0.01		0.28
Part B	24042.50**	4679.47	<0.01		0.18
Outpatient	4030.75	2538.63	0.11		0.68
Physician fee schedule	15342.84**	2187.90	<0.01		0.10*
Others	4668.91**	1665.29	0.01		0.13
Part D	1197.74	1139.67	0.29		0.10*
Healthcare utilization					
# of hospitalizations	0.83	0.58	0.15		0.73
# of ED visits	-1.89**	0.76	0.01		0.04**
# of outpatient visits	-4.18	3.10	0.18		<0.01**
# of physician visits	82.47**	11.19	<0.01		0.18
# of prescription claims	-53.54**	13.97	<0.01		0.40

Table A44. Continued

90-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.05	0.12	0.69	25.64	0.16
Total healthcare cost	54248.81**	9837.74	<0.01		0.07*
Part A	33509.13**	7218.91	<0.01		0.24
Part B	19082.21**	3675.19	<0.01		0.02**
Outpatient	3151.37	2067.70	0.13		0.14
Physician fee schedule	11228.36**	1617.87	<0.01		0.02**
Others	4702.49**	1359.97	<0.01		0.58
Part D	1657.47	936.32	0.08		0.28
Healthcare utilization					
# of hospitalizations	0.68	0.46	0.14		0.50
# of ED visits	-0.99	0.60	0.10		0.70
# of outpatient visits	-0.56	2.47	0.82		0.01**
# of physician visits	58.86**	8.06	<0.01		<0.01**
# of prescription claims	-26.36**	10.37	0.01		0.02**

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
ED (emergency department);
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Table A44. Continued

Notes:
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.
**significant at 95% CI; *significant at 90% CI;
Chow F-tests examined whether the instruments described a statistically significant portion of variation in depression diagnosis. A "rule of thumb" for a strong instrument relationship is a Chow F-value > 10.[213]
Hansen over-identification tests were used to examine whether excluding the area diagnosis ratio (ADR)-based instruments from the second stage of 2SLS was appropriate (null hypothesis)[214]

Table A45. Instrumental variables estimates of the effectiveness of depression diagnosis among elderly patients with acute myocardial infarction (Area diagnosis rates by excluding a patient from the calculation of that patient's area unadjusted diagnosis ratios, 150-person area, quintile)

30-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.14	0.19	0.45	17.34	0.84
Total healthcare cost	28654.23**	14703.36	0.05		0.10*
Part A	9284.57	11347.41	0.41		0.25
Part B	14013.59**	5162.57	0.01		0.08*
Outpatient	-3675.42	2917.30	0.21		0.07*
Physician fee schedule	15302.89**	2726.43	<0.01		0.09*
Others	2386.12	1964.67	0.23		0.36
Part D	5356.08**	1693.45	<0.01		0.64
Healthcare utilization					
# of hospitalizations	-0.45	0.77	0.56		0.91
# of ED visits	-2.64**	1.01	0.01		0.65
# of outpatient visits	-1.01	4.14	0.81		0.09*
# of physician visits	91.37**	14.97	<0.01		0.03**
# of prescription claims	29.45*	17.84	0.10		0.05**

Table A45. Continued

60-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	-0.17	0.17	0.30	16.67	0.56
Total healthcare cost	52758.97**	13847.94	<0.01		0.74
Part A	26920.03**	10069.87	0.01		0.67
Part B	21868.30**	5404.56	<0.01		0.63
Outpatient	1820.38	3174.47	0.57		0.21
Physician fee schedule	15516.62**	2575.97	<0.01		0.76
Others	4531.30**	1839.45	0.01		0.33
Part D	3970.65**	1420.33	0.01		0.32
Healthcare utilization					
# of hospitalizations	0.38	0.67	0.58		0.62
# of ED visits	-1.67**	0.86	0.05		0.87
# of outpatient visits	-3.82	3.60	0.29		0.01**
# of physician visits	97.68**	14.57	<0.01		0.36
# of prescription claims	-4.09	14.85	0.78		0.50

Table A45. Continued

90-day observation window	Estimate	Standard error	P value	Chow test (F value)	Hansen test (P value)
Survival	0.08	0.13	0.53	22.96	0.17
Total healthcare cost	41990.25**	9620.95	<0.01		0.53
Part A	23512.20**	7192.48	<0.01		0.67
Part B	14550.02**	3376.66	<0.01		0.38
Outpatient	-229.72	1779.15	0.90		0.61
Physician fee schedule	10511.85**	1655.63	<0.01		0.05**
Others	4267.89**	1332.57	<0.01		0.15
Part D	3928.03**	1093.59	<0.01		0.99
Healthcare utilization					
# of hospitalizations	0.58	0.48	0.23		0.95
# of ED visits	-1.00*	0.61	0.10		0.90
# of outpatient visits	-1.36	2.55	0.59		<0.01**
# of physician visits	63.17**	8.87	<0.01		0.01**
# of prescription claims	24.74**	10.73	0.02		<0.01**

Notes:

All models adjusted for patient demographic characteristics, pre-index medical conditions, therapy/procedures, medication use, and contextual factors;
ED (emergency department);
Total healthcare cost is a continuous variable by summing up standardized Medicare reimbursements to all providers over the 1 year period post (the index date + 30/60/90 days) or till death, including Medicare Part A, B, and D payments. The standardized Medicare payments adjusted the actual payments to remove the differences in the geographic and facility-type payments due to Medicare policy that allows direct and accurate comparison of healthcare resource use;

Table A45. Continued

Notes:
Part A cost summed up all standardized payments from inpatient, skilled nursing facility, home health agency, and hospice claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part B cost summed up all standardized payments from outpatient, carrier claims (including physician and other provider fee schedules), and durable medical equipment claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Part D cost summed up all standardized payments from prescription claims over the 1 year period post (the index date + 30/60/90 days) or till death;
Hospitalizations were based on the number of inpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
ED visits were based on the number of inpatient/outpatient claims at emergency rooms over the 1-year period post (the index date + 30/60/90 days) or till death;
Outpatient visits were based on the number of outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Physician visits were based on the number of carrier claims and outpatient claims over the 1-year period post (the index date + 30/60/90 days) or till death;
Prescription claims were based on the number of prescription claims over the 1-year period post (the index date + 30/60/90 days) or till death.
**significant at 95% CI; *significant at 90% CI;
Chow F-tests examined whether the instruments described a statistically significant portion of variation in depression diagnosis. A "rule of thumb" for a strong instrument relationship is a Chow F-value > 10.[213]
Hansen over-identification tests were used to examine whether excluding the instruments from the second stage of 2SLS was appropriate (null hypothesis)[214]

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