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Depression and Benign Prostatic Hyperplasia in Elderly Male Medicare Beneficiaries

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DEPRESSION AND BENIGN PROSTATIC HYPERPLASIA IN ELDERLY MALE MEDICARE BENEFICIARIES

by

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DEDICATION

This dissertation is dedicated to my wife, Iby and kids, Obed, Joni and Olivia, who have been a great source of support and encouragement to me as I faced the challenges of graduate school. I am truly thankful for having all of you in my life. Finally, I give all the Glory to God Almighty for His saving grace in my life.

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Abstract

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Depression is a common cause of disability and mortality in the elderly population. Benign prostatic hyperplasia (BPH), a benign enlargement of prostate gland, may be related to depression in men, as reported in previous studies. This dissertation explored the co-occurrence of depression and BPH in elderly men, the transition probabilities of depression status as its relations to varying BPH transition status, and the effect of socioeconomic disadvantage on depression in men with BPH. The data were drawn from the Medicare Current Beneficiary Survey (MCBS) and Medicare claims data from 2005 through 2009. The study population comprised of community dwelling elderly male Medicare beneficiaries aged 65 years or above (N=10, 067). Depression and BPH were defined using both self-report and diagnostic codes. Two transition processes for depression and BPH were constructed based on two follow-up years. The Markov process for depression and BPH states progression and their probabilities were determined. The transition rates were assessed using generalized linear mixed models with covariance matrix estimated by generalized estimating equations to explain the variations between repeated measures. Survey weights and multilevel cluster effect was considered in all our analysis. We adjusted for age, race, marital status, education level, income levels, insurance coverage, and comorbidities including cancer, diabetes, heart diseases, arthritis, and other mental health conditions. We found an overall prevalence of 13% for depression and about 41% for BPH. The adjusted risk ratio

(ARR) of depression in men with BPH compared with no BPH was 1.16 (95% CI, 1.04-1.30). Compared to those who remained with no-BPH, there was about 50% more chances of transiting from depression to no depression state in men who progressed from BPH to no-BPH status, (Adjusted transition rate, 1.49; 95% CI, 1.05-2.12;p-values= 0.021). The probability of transition from no-depression to depression in elderly men with two or more comorbidity was about two-folds higher compared with no comorbidity. Heterogeneity in socioeconomic context is a significant determinant of depression risk in elderly men with BPH. In conclusion, a significant impact of BPH on depression was reported. There is need to sensitize healthcare professionals on the importance of carefully depression evaluation among elderly men.

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LIST OF ABBREVIATIONS

DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition	1
WHO	World Health Organization	1
BPH	Benign Prostatic hyperplasia	1
ADAMS	Aging, Demographic and Memory Study	2
NHANES	National Health and Nutritional Examination Survey	2
LUTS	Lower Urinary Tract symptoms	4
PHQ-9	Patient Health Questionnaire-9	6
GDS	Geriatrics Depression Scale	6
COPD	Chronic Obstructive Pulmonary Disease	4
ICD-9	International Classification of Diseases Ninth Revision	6
AUA-SI	Urological Association Symptom Index	6
IPSS	International Prostate Symptom Score	6
CMS	Centers for Medicare & Medicaid Service	10
MCBS	Medicare Current Beneficiary Survey	10
ARR	Adjusted Risk Ratio	20
ATR	Adjusted Transition Risk Ratio	37

CHAPTER 1

INTRODUCTION

Background

Depression in late life, defined as having depressive symptoms in adults aged 65 or older, is a severe and common mental health condition in the elderly population (American Psychiatric Associations Diagnostic and Statistical Manual (DSM-IV)) [1-4]. In the United States, nearly 7 million of the 31 million elderly over 65 years are affected by depressive symptoms [5]. About 10–12% of the medically ill older adult suffers from major depression [6]. However, depression is often under-diagnosed or undertreated in primary care settings [7, 8]. The World Health Organization (WHO) reports that symptoms of depression in older people are commonly overlooked or untreated because they coincide with other late life medical conditions [8]. Meanwhile, under-recognition of depression in late life can lead to worse outcomes of preexisting medical illnesses, other emotional sufferings, quality of life and risk of disability [9-11]. For example, elderly people with depression have other chronic medical conditions such as diabetes, arthritis, cardiovascular diseases and cancer, as well as neurological conditions like dementia and/or Alzheimer's disease, all of which are generally referred to comorbidities [12-16]. Of these comorbidities, benign prostatic hyperplasia (BPH) may be a significant cause of morbidity and emotional suffering in elderly men and negatively affect health quality of life of aging men, which may lead to depressive symptoms [17-20]. A recent report showed an improvement in recognizing depression among the nursing homes residents [21]. Nevertheless, the association of aging with multiple chronic medical conditions has

led to missed opportunities for early detection of depressive illness in the primary care settings [22-29].

Epidemiology of depression

Depression is a mood disorder, characterized by feeling of sadness and diminished interest in life [15, 30]. It is also associated with abnormal physical and other mental changes such as weight gain or loss, psychomotor agitation or retardation, fatigue, inappropriate guilt, concentration difficulties, as well as recurrent thoughts of death [31]. Older people with depression typically report more symptoms of physical weakness and insomnia than other age groups [15, 32, 33].

The prevalence of depression among the elder population varies among studies, regions, and dwelling status [4, 33-39], ranging from 10 to 15% per year in the US elderly population [40-46]. A report from the Aging, Demographic and Memory study (ADAMS), drawn from Health and Retirement Study, estimated the overall prevalence of depression in the general older population at 11.2%, and about 10.2% among elderly men [46]. The National Health and Nutrition Examination Survey (NHANES) conducted from 2007 to 2010, estimated the prevalence of current depression in males aged 60 years or above at approximately 5% [47]. This does not contradict the above US prevalence as NHANES measures the point prevalence of depression among community dwellers. However, studies conducted among elderly Australians reported a significantly lower prevalence of 2- 8%, partly due to different tools used in assessing depression symptoms [48, 49].

Compared with community dwellers, the risk of depression among older population living in institutional facilities such as nursing homes and long-term care

facilities is about two folds higher [4, 15, 44, 49-56]. Studies have argued that coexisting psychiatric illnesses is the predominant cause of high risk of depression among those in the institutional settings [1, 4, 48, 51, 57-59]. Although reports have shown that older individuals underutilize mental health facilities [60-63], depression is significantly associated with increased healthcare services utilization among adult population [2, 64-66]. Egede and colleagues have shown that the coexistence of major depression with common chronic medical conditions is associated with significantly greater odds of ambulatory care visits, emergency department visits, days spent in bed due to illness and functional disability [67, 68].

Risk factors for depression in the elderly

Depression in the elderly results from complex interactions among individual, environmental and genetic predisposing factors. Individual and environmental factors are the leading determinants of depression in the elderly [69]. Factors that influence depression among the elderly can be generally classified into: (1) Socioeconomic status such as race/ethnicity, marital status, education, income level, and residence; (2) Medical conditions such as chronic diseases, mental health illnesses and organic brain diseases (e.g. cognitive impairment and Alzheimer's disease); (3) Adverse life events such as loss of job and bereavement, and (4) Family history of depression [69-74].

Depression prevalence varies across race and socioeconomic groups [75-78]. The risk of depression is higher in White (11.7%) and Hispanic (12.5%) elderly population compared to Blacks (4%) [46]. Further, there is a higher prevalence of depression in older people residing in urban locations compared to those in the rural locations [75-78]. Studies also suggest that uninsured or underinsured elderly people are at higher risk of

depression. For instance, studies have found that underinsured Medicare beneficiaries were undertreated for depression because of partial coverage and high copay for mental health treatment [64, 79-82].

Studies have consistently demonstrated that depression is frequent among elderly people with chronic diseases such as diabetes, cancer, arthritis, cardiovascular disease and chronic obstructive pulmonary disease (COPD) [83-91]. When people age, these chronic diseases occur, partly due to aging process and also due to cumulative effects of different risk exposures. Even though depression is not a process of aging, advanced age has been linked with a higher risk of depression, which may be explained by their high susceptibility to chronic medical conditions, physical disability and cognitive decline [4, 78, 92].

Epidemiology of benign prostatic hyperplasia

BPH is a non-cancerous enlargement of the prostate gland associated with aging in men [93-96]. It is the major cause of lower urinary symptoms (LUTS) in men [97-101]. Although BPH is a slowly progressing disease, detection rate has increased in aging men because of the growing awareness of prostate cancer screening [100, 102]. The prevalence of BPH among men over 65 years ranges from 20% to 60% [102-106]. Common symptoms of LUTS include increased bladder outlet obstruction, urinary frequency, urgency, hesitancy, incomplete emptying, weak urinary stream and frequent urination at night [107-111]. These symptoms can negatively affect the quality of life of aging men with BPH [101, 105, 110, 112, 113]. Despite that much research has been done about BPH, the pathophysiologic mechanism of BPH is still unclear. Some mechanisms have been linked to stimulation of growth of the prostate gland in aging

men. The immune-inflammatory pathway may promote prostate tissue growth through activation of growth factors [114-121]. In addition, the action of the active metabolite of testosterone hormone (e.g., dihydrotestosterone, DHT) following hormonal alteration has been reported in the older men [122, 123]. While the level of overall testosterone reduces in aging in men, the DHT and the androgen receptor (AR) levels remain relatively high [124].

Co-occurrence of depression and benign prostatic hyperplasia in aging men

Studies that explored the relation between depression and BPH in aging men are scarce. Up till now, only six articles have explored this association in the general male population, which include five cross sectional studies and one retrospective cohort study [108, 125-129]. These studies suggest a consistent and significant increased risk of depression among elderly people with BPH or LUTS. One study also demonstrated that compared with Blacks, the odds of depressive symptoms was high among White men with LUTS (OR 2.60, 95% CI 1.39–4.85, $p < 0.01$), and Hispanic men with LUTS (OR 4.14, 95% CI 1.15–14.95, $p < 0.05$) [127]. Still, the mechanism between depression and BPH is unclear. A common inflammatory pathway may play a role in this relationship [108].

However, methodological concerns and limited adjustment for confounding factors raise issues regarding the interpretation of these findings. For instance, Huang et al., 2011, drew their sample from mostly outpatient population (ambulatory care visits), therefore there may have been a possible surveillance bias among patients with BPH [125] and the study did not control for confounding effect of coexisting medical conditions. The remaining studies comprised of men below the ages 65 years [108, 125,

129, 130]. Only two studies, conducted in the same population of elderly Chinese men, limited their analysis to older individuals with age 65 years or above [126, 128]. One study was conducted in a clinical setting [108].

The most common instruments used to define BPH/LUTS in these studies were American Urological Association Symptom Index (AUA-SI) or the International Prostate Symptom score (IPSS) instrument [108, 125, 126, 128-130]. The AUA Symptom Index (identical to the seven symptom questions of the International Prostate Symptom Score) is used for early assessment of patients suspected with BPH symptoms [131]. The AUA-SI scores are categorized as having mild (score 0 to 7), moderate (8 to 19), and severe (20 to 35) LUTS. Overall, watchful waiting strategy is the standard management for patients suspected of having early BPH [104, 110, 132, 133].

On the contrary, the instruments used to measure depression varied across studies. They include the Geriatric depression scale (GDS), Center for Epidemiologic Studies Depression Scale (a validated questionnaire from the Massachusetts Male Aging Study), the NHANES Patient Health Questionnaire-9 (PHQ-9), and International Classification of Diseases Ninth Edition (ICD-9) diagnostic codes [108, 125, 126, 128-130]. These instruments may vary in their sensitivity and specificity, thus influence the finding observed in the different studies.

Other methodological issues also exist. For example, the retrospective study by Huang et al., 2011, that examined the induction time for depression in men with BPH had some methodological limitations because information of censored participants had been omitted [125]. Furthermore, by stratifying the analysis by age group, their study had low power to detect significant effect because of the small sample size [134].

In spite of the methodological issues, previous studies provide a framework and foundation to better examine the association between BPH and depression in aging men. A thorough understanding of the burden of depression and the transition of depression status with BPH health states in elderly men is important to elucidate the causal sequence between BPH and depression. Therefore, it is beneficial to conduct a study using a more rigorous technique to explore this relationship. We propose to use data from a nationally representative population with diverse socio-demographic and models controlling for factors known to influence the occurrence of depression in elderly population.

Study Rationale

Increasing life expectancy results in a growing elderly population in both the US and around the world. Consequently, there is a significant rise in the burden of depression and chronic medical conditions. Under-detection and under treatment of depression may lead to disability and poor quality of life in older people. There is a gap in our understanding of how BPH might influence risk of depression in older male population. In addition, it is not well understood whether BPH is a sufficient cause to increase the risk of depression or a combined effect of BPH with other comorbidities or socioeconomic context. No previous study has examined the transition probabilities between depression and BPH states in elderly men. To examine the transition states, the Markov transition model technique is the most appropriate approach and provides information on the time sequence and causal inference between depression and BPH.

The main objectives of this study are: (1) To describe the epidemiology of depression and BPH occurrence among elderly male Medicare beneficiaries in the United States enrolled between years 2005 and 2009. (2) To determine the transition

probabilities of depression states and their relation to the changes of BPH status in elderly men during the two years of follow up. (3) To examine the impact of socioeconomic disadvantages on depression in elderly men with BPH.

Conclusion

A thorough understanding of the burden of depression in elderly male population is critical and necessary for targeted intervention. The results from this research will facilitate effective health planning and policy change. Furthermore, understanding the effect of socioeconomic disadvantage on depression in elderly men with BPH will address health disparity and allocate limited health resources more efficiently.

CHAPTER 2

CO-OCCURRENCE OF DEPRESSION AND BENIGN PROSTATIC HYPERPLASIA IN ELDERLY MEN

Introduction

Depression is a common psychiatric problem with serious consequences in the elderly population [1, 2, 4, 15, 78, 135]. The prevalence of depression among elderly community dwellers is approximately 8-15%, with an estimated prevalence of about 10% in the primary healthcare settings [4, 8, 136-138]. Reports show that depression in the elderly is often either under-recognized or undertreated [8, 139]. In addition to the aging process as a predisposing factor, several studies have suggested a significant relationship between chronic medical conditions and depression among the aging population [3, 13, 15, 140, 141]. For instance, medical conditions such as cardiovascular diseases, diabetes mellitus, chronic obstructive airway diseases, cancer, and arthritis are associated with an increased risk of depression occurrence [16, 39, 59, 142-146]. However, Krishan et al, 2002, noted that reverse association may exist between depression and medical conditions like heart diseases, cancer, arthritis and diabetes [13].

There is limited epidemiologic research on the relation between depression and benign prostatic hyperplasia (BPH), a non-cancerous enlargement of the prostate, in elderly men. Findings from recent studies suggest that BPH may be associated with an increased risk of depression among men [108, 126-129]. However, the mechanism underlying this relationship is unclear. An inflammatory mechanism may be a possible common pathway [108]. BPH can cause significant health problems that negatively impact the quality of life of aging men [86, 102, 119, 148, 149]. It affects between 20 to

60% of elderly men and commonly presents with distressing lower urinary tract symptoms (LUTS) [148-151], including poor urinary stream, hesitancy, terminal dribbling and incomplete voiding. The bothersome LUTS symptoms could be responsible for the increased risk of depression in this population [20, 152, 153]. Two studies of the association between LUTS and depression among Chinese men with age of 65 year or above, found that depression risk was higher among men experiencing LUTS compared to those with no LUTS [126, 128]. However, this study did not fully capture the influence of other comorbidities on depression.

The objective of this study is to examine the risk of depression in elderly men aged 65 years or above with BPH, controlling for effects of comorbidities and other socio-demographic determinants of depression. The current study analyzes data from the Medicare Current Beneficiary Survey (MCBS), a national representative sample of US elderly population, and the accompanying Medicare claims data from 2005 to 2009.

Materials and methods

Data from MCBS and the Medicare claims data from 2005 through 2009 were combined. The study population comprised of elderly men 65 years or above. The MCBS is nationally representative study conducted by the Center for Medicare and Medicaid Services (CMS). The survey participants are recruited every fall to replenish one third of MCBS sample, thus forming a yearly cohort. They will be followed up for three years. Every year there will be three rounds of interviews in which extensive questionnaires are used to solicit information including socioeconomic status, health status, health care utilization and medication use. We extracted information about depression and BPH from personal health interviews conducted among elderly men living in the community

and from the claims data using the International Classification of Disease, version nine (ICD-9) codes. We used Medicare Part A (inpatients claims), outpatient claims, and Part B (claims for physicians and other services) from 2005 to 2009 to identify clinical cases of depression and BPH.

Outcome Measure

Depression: The health status survey questionnaire has two questions related to depression symptoms. The first question is whether the respondent was sad or depressed in the past 12 months ("all of the time", "most of the time", "some of the time", "a little of the time" and "none of the time"). The second question is whether they had loss of interest in the past 12 months ('yes" or "no"). We defined depression as follows: (1) Any respondent who reported having been sad or depressed "all of the time" or "most of the time"; (2) sad or depressed "some of the time" and also loss of interest, and (3) clinically diagnosed depression, i.e., having the ICD-9 codes for depression from the claims data. The ICD-9 codes used to extract unipolar depression, based on prior studies, were 296.2 (major depressive disorder, single episodes), 296.3 (major depressive disorder, recurrent episodes), 300.4 (neurotic depression), 309.0 (Adjustment disorder with depressed mood), 309.1 (prolonged depressive reaction), and 311 (depression, not elsewhere classified). [79] This consolidated definition of depression with the above methods (claims data and survey questions) enabled us to identify all cases diagnosed clinically and those probably under-reported depression cases [155]. After crosschecking the cases of depression between the survey and claims data, we observed that about 6% of elderly men who reported depression in the survey were not clinically diagnosed while 2% of people with clinical depression did not report such in the survey

Main predictor

Benign prostatic hyperplasia (BPH): We identified BPH cases from responses to the question on whether "Past year respondent was told he had enlarged prostate/BPH" ("yes" or "no"). We also identified clinically diagnosed BPH using the ICD-9 codes from the claims data. The ICD-9 codes according to Urologic disease in America's recommendation [101] were: 594.1 (Other calculus in bladder), 599.6 (Urinary obstruction), 599.60 (Urinary obstruction, unspecified), 600 (hyperplasia of the prostrate), 788.2 (Retention of urine), and 788.4 (Frequency of urination and polyuria). Finally, we crosschecked the responses to the questions and physicians diagnosis and found that 12% of respondent who self-reported BPH where not clinically identified from the claims data, while 15% of people with confirmed BPH by the physicians did not report such in the survey.

Covariates

Comorbidities: the health survey provided information on the following medical conditions: cancer, heart disease, diabetes mellitus, arthritis and mental health illness excluding depression. Respondents were asked whether in the past year, a doctor ever told them they had the above diseases or conditions. We categorized the responses as yes or no to any of the questions. We also created a summary variable called total comorbidity that is the sum of coexisting medical illness listed above.

Socio-demographic covariates from survey data included and classified: age group (65 – 69, 70 – 74, 75 – 79, 80 – 84 and 85+), race (White, Black, other), marital status (Married, Widowed, Divorced/separated, and other), education (Less than high school, High school, and College certificates or above). Other variables include income

level (Less than $15,000, $15,001 - $25, 000, and More than $25, 000), and insurance coverage (Medicare only, Medicare and Employer-Sponsored Insurance (ESI), Medicare and Self-purchased (SP), and all three types of insurance). Variables that are reported as refused to answer or with no value were treated as missing values. No additional missing imputation was employed given the small percentage of missing.

Statistical Analysis

Analysis was restricted to community dwelling elderly men ages 65 years or above. We excluded the following respondents from our analysis hierarchically: those with prostate cancer (n=133), and those with end-stage renal failure because of similarity with symptoms of BPH (n = 5). Descriptive statistics was performed for the overall study population and stratified by survey year using the SURVEYFREQ procedure in SAS. Risk ratios were estimated using generalized linear mixed models with covariance matrix estimated by generalized estimating equations (GEE) to explain the variation between repeated measures (PROC GENMOD in SAS). We accounted for the complex sampling design by incorporating the multilevel clusters and weight variables into all analysis. The final model for the multivariate analyses was selected using the QIC (Quasi-likelihood under the independence model criterion) analogous to the AIC (Aikaike's Information Criterion) statistics used for comparing model fits because the GEE method is not a likelihood-based method and does not provide the AIC. The smaller QIC statistics is preferred. QIC fit statistics provides working correlation structure for a given model [156, 157]. We also stratified our analysis by year of survey, number of comorbidities and the types of comorbidities. Finally, we conducted subset analyses using depression and BPH information from the claims data only or self-report only to examine effects of

underreporting. All analyses was done using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

The survey included 10, 067 community dwelling male MCBS participants, aged 65 years or above, from 2005 through 2009. The average age was 76 years, and the maximum was 101 years. Table 1 shows the summary of respondents' characteristics. The prevalence pooled over three years was 13% for depression and about 41% for BPH. The majority of the participants were Non-Hispanic Whites population (87%) and over two-thirds of the respondents were currently married. Nearly 44% had college level certificates and 61% had annual income levels of greater than $25, 000.00. In addition to Medicare insurance, 64% had other private insurance coverage (Self-Purchased, Employer-Sponsored or both). Heart diseases (55%) such as congestive heart failure, heart valve diseases, and myocardial infarction, are the most common medical condition, followed by cancers (30%) excluding prostate and skin cancer. About 70% of the study sample had one or more coexisting comorbidities.

Table 2 provides a description of study sample by year of survey. From 2005 through 2009, the annual prevalence of depression was approximately 9% and the annual prevalence of BPH ranged from 32% to 36%. The proportion of elderly men aged 85 years and above increased from 8.7% in 2005 to 10.4% in 2009. There was no difference in the proportion of individuals sampled by race during the survey period and over two-third of the surveys were White non-Hispanics. The proportion of elderly men with less than high school education decreased slightly over time from 26% to 22% while those with college education increased from 42 to 46% (p-value <.0001). In addition, the

proportion with income greater than $25, 000.00 increased from 58% in 2005 to 64% in 2009. The prevalence of diabetes mellitus (p-value <.0001) and heart diseases (p-value = 0.2086) increased during the five years and other mental health conditions (excluding depression) decreased from 9% to about 2% (p-value <.0001) .

Multivariate analysis of the relationship between depression and BPH adjusted for survey year, age group, race, marital status, education, income, insurance and number of comorbidities is shown in Table 3. There was a significant increase of the risk of depression with BPH compared with no BPH (Adjusted risk ratio (ARR), 1.16; 95% CI, 1.04-1.30; p-value = 0.005). Those surveyed in year 2006 and 2007 had significantly higher risk of depression compared to with 2005 (ARR, 1.20; 95% CI, 1.05-1.36 and ARR, 1.19; 95%CI, 1.05-1.35, respectively). The results also show that older age groups over 69 years compared with 65 to 69 years old is associated with significantly higher risk of depression (Table 3). Widowed and divorced/separated marital status compared with married were associated with a higher risk of depression (ARR, 1.50; 95% CI, 1.30-1.73 and ARR, 1.32; 95%CI, 1.09-1.59 respectively), while an education level of high school or above compared with less than high school, as well as annual income level more than $25, 000 compared with less than $15,000 were significantly associated with lower risk of depression. The risk of depression also significantly increased with the number of comorbidities. No significant difference was found among race and types of insurance coverage.

Table 1. Description of study sample of men ages 65 years and greater: Medicare Current Beneficiary Survey (MCBS), 2005– 2009 pooled.

Variables	N = 10, 067	Weighted percentage
Ever depressed in three years	1, 432	13.0
Benign prostatic hyperplasia	4, 493	40.6
Survey year		
2005**	3, 914	33.0
2006	1, 644	15.9
2007	1, 716	17.7
2008	1, 564	17.6
2009	1, 229	15.7
Race/Ethnicity		
White Non-Hispanics	8, 826	86.9
Black Non-Hispanics	720	7.7
Hispanics	213	2.0
Other	308	3.5
Age in years		
65 – 69	2, 518	35.1
70 – 74	2, 411	23.5
75 – 79	1, 878	18.0
80 – 84	1, 773	13.1
85+	1, 487	10.3
Marital status		
Married	7, 209	73.2
Widowed	1, 580	13.2
Divorced/separated	939	9.9
Other	339	3.8
Education		
Less than high school	2, 630	24.2
High school	3, 207	31.6
College	4, 230	44.3
Income level		
Less than $15,000	805	7.8
$15,000 - $25, 000	3, 334	31.7
More than $25, 000	5, 928	60.5
Comorbidity		
Diabetes	2, 732	27.0
Arthritis	472	4.1
Cancer	3, 218	29.6
Heart disease	5, 788	54.5
Mental Health	1, 033	9.5

Table 1 (continued). Description of study sample of men ages 65 years and greater: Medicare Current Beneficiary Survey (MCBS), 2005– 2009 pooled.

Variables	N = 10, 067	Weighted percentage
Insurance coverage		
Medicare only	3, 572	36.3
ESI[a]	3, 486	35.2
SP[b]	2, 289	21.5
ESI and SP[c]	720	7.1
No. of interviews		
1	4, 129	49.3
2	2, 637	22.9
3	3, 301	27.8
Total Comorbidities		
0	2, 790	29.3
1	4, 028	39.8
2 or more	3, 247	31.0

[a] Employer Sponsored Insurance (ESI) and Medicare
[b] Self-purchased (SP) insurance and Medicare
[c] Employer sponsored, self-purchased and Medicare insurance
**2005 has larger sample size because it also includes 2004 cohort.

Table 2. Description of study sample by year of survey.

Variables	2005 N = 3, 914 (%)	2006 N = 3, 897 (%)	2007 N = 3, 994 (%)	2008 N = 3, 967 (%)	2009 N = 3, 240 (%)
Ever depressed in past year	365 (8.9)	387 (9.5)	367 (8.8)	373 (9.0)	300 (9.0)
Benign prostatic hyperplasia	1, 435 (35.0)	1, 492 (36.4)	1, 527 (36.2)	1, 402 (33.4)	1, 112 (32.0)
Race/Ethnicity					
White Non-Hispanics	3, 434 (87.5)	3, 428 (87.5)	3, 517 (87.6)	3, 511 (87.3)	2, 854 (87.4)
Black Non-Hispanics	292 (7.7)	267 (7.3)	278 (7.4)	261 (7.5)	226 (7.6)
Hispanics	79 (1.9)	86 (2.0)	94 (2.2)	86 (1.9)	64 (1.7)
Other	109 (3.0)	116 (3.2)	105 (2.8)	109 (3.3)	96 (3.3)
Age in years					
65 – 69	995 (31.6)	963 (31.2)	953 (31.4)	949 (32.0)	822 (33.5)
70 – 74	893 (23.6)	914 (24.4)	945 (25.0)	955 (24.6)	783 (24.9)
75 – 79	834 (21.9)	811 (21.1)	793 (19.6)	760 (18.8)	609 (18.3)
80 – 84	706 (14.2)	717 (14.3)	762 (14.3)	741 (14.2)	556 (12.9)
85+	486 (8.7)	492 (9.1)	541 (9.7)	562 (10.4)	470 (10.4)
Marital status					
Married	2, 841 (73.9)	2, 826 (73.5)	2, 888 (73.5)	2, 824 (72.5)	2, 313 (72.6)
Widowed	627 (13.9)	604 (13.6)	608 (13.2)	637 (14.0)	499 (13.3)
Divorced/separated	335 (9.0)	329 (9.0)	371 (9.9)	378 (10.1)	333 (10.9)
Other	111 (3.3)	138 (4.0)	127 (3.4)	128 (3.5)	95 (3.3)
Education					
Less than high school	1, 076 (26.2)	1, 071 (26.4)	1, 040 (24.5)	999 (23.3)	798 (22.4)
High school	1, 272 (32.3)	1, 231 (32.1)	1, 294 (32.6)	1, 273 (31.8)	1, 029 (31.4)
College	1, 566 (41.5)	1, 595 (41.6)	1, 660 (42.9)	1, 695 (44.8)	1, 413 (46.1)
Income level					
Less than $15,000	346 (8.8)	298 (7.4)	307 (7.7)	291 (7.0)	242 (7.0)
$15,000 - $25, 000	1, 350 (33.1)	1, 313 (32.7)	1, 267 (30.5)	1, 231 (30.2)	1, 007 (29.7)
More than $25, 000	2, 218 (58.2)	2, 286 (60.0)	2, 420 (61.8)	2, 445 (62.9)	1, 991 (64.3)

Table 2 (Continued). Description of study sample by year of survey.

Variables	2005 N = 3, 914 (%)	2006 N = 3, 897 (%)	2007 N = 3, 994 (%)	2008 N = 3, 967 (%)	2009 N = 3, 240 (%)
Comorbidity					
Diabetes	845 (21.4)	896 (23.1)	1, 002 (25.3)	1, 084 (27.3)	923 (28.0)
Arthritis	104 (2.5)	111 (2.8)	105 (2.4)	110 (2.5)	77 (2.2)
Cancer	1, 144 (27.6)	1, 157 (28.1)	1, 217 (28.8)	1, 208 (28.5)	940 (26.8)
Heart disease	1, 886 (47.8)	1, 932 (48.2)	2, 021 (49.2)	2, 005 (49.6)	1, 663 (50.7)
Mental Health	352 (9.2)	303 (7.8)	331 (8.0)	329 (8.0)	42 (1.5)
Insurance coverage					
Medicare only	1, 256 (32.5)	1, 237 (32.4)	1, 362 (35.0)	1, 427 (36.9)	1, 264 (39.1)
ESI[a]	1, 348 (34.5)	1, 375 (35.4)	1, 401 (35.4)	1, 375 (35.0)	1, 117 (35.4)
SP[b]	1, 014 (24.9)	952 (23.5)	908 (21.8)	863 (20.7)	658 (19.4)
ESI and SP[c]	296 (8.1)	333 (8.7)	323 (7.8)	302 (7.4)	201 (6.1)
Total Comorbidities					
0	1, 141 (30.5)	1, 104 (29.7)	1, 088 (28.7)	1, 046 (27.8)	895 (29.0)
1	1, 603 (40.0)	1, 582 (40.4)	1, 566 (39.1)	1, 556 (39.2)	1, 310 (40.6)
2 or more	1, 170 (29.5)	1, 211 (29.9)	1, 340 (32.2)	1, 365 (33.1)	1, 035 (30.5)

[a] Employer Sponsored Insurance (ESI) and Medicare
[b] Self-purchased (SP) insurance and Medicare
[c] Employer sponsored, self-purchased and Medicare insurance

Table 3. Multivariate analysis of determinants of depression in elderly male Medicare beneficiaries.

Variables	ARR	95% C.I	p-value
Benign prostatic hyperplasia			
No (Ref)	-	-	-
Yes	1.16	1.04 – 1.30	0.010
Survey year			
2005 (Ref)	-	-	-
2006	1.20	1.05 – 1.36	0.006
2007	1.19	1.05 – 1.35	0.007
2008	1.00	0.86 – 1.16	0.980
2009	0.84	0.69 – 1.03	0.088
Race/Ethnicity			
White Non-Hispanics (Ref)	-	-	-
Black Non-Hispanics	0.88	0.70 – 1.10	0.264
Hispanics	0.86	0.62 – 1.19	0.360
Other	1.11	0.77 – 1.59	0.582
Age in years			
65 – 69	-	-	-
70 – 74	1.19	0.98 – 1.45	0.080
75 – 79	1.44	1.19 – 1.74	0.001
80 – 84	1.27	1.02 – 1.58	0.034
85+	1.37	1.12 – 1.68	0.002
Marital status			
Married (Ref)	-	-	-
Widowed	1.50	1.30 – 1.73	< 0.0001
Divorced/separated	1.32	1.09 – 1.59	0.004
Other	1.10	0.68 – 1.77	0.708
Education			
Less than high school (Ref)	-	-	-
High school	0.78	0.69 – 0.90	0.001
College	0.68	0.59 – 0.79	< 0.0001
Income level			
Less than $15,000 (Ref)	-	-	-
$15,000 - $25, 000	0.96	0.79 – 1.16	0.669
More than $25, 000	0.70	0.57 – 0.85	0.001
Insurance coverage			
Medicare only (Ref)	-	-	-
ESI	1.02	0.90 – 1.15	0.802
SP	0.94	0.79 – 1.11	0.444
ESI and SP	0.94	0.74 – 1.19	0.602
Total Comorbidities			
0 (Ref)	-	-	-
1	1.31	1.10 – 1.54	0.002
2 or more	2.07	1.74 – 2.46	< 0.0001

Multivariate analysis of determinants of depression in elderly Medicare beneficiaries stratified by number of comorbidities is shown in table 4.The risk of depression among BPH compared with no BPH was significant among respondents without any comorbidity (ARR, 1.44; 95% CI, 1.12-1.86). In addition, among those with two or more comorbidities the risk of depression in those with BPH was about 18% higher (ARR, 1.18; 95% CI, 1.02- 1.38) compared with no BPH.

Table 4. Multivariate analysis of determinants of depression in elderly Medicare beneficiaries stratified by number of comorbidities.

	Number of comorbidities		
	None, n = 2, 790	1, n = 4, 028	>= 2, n = 3, 247
Variables	ARR (95% C.I)	ARR (95% C.I)	ARR (95% C.I)
Benign prostatic hyperplasia			
No (Ref)	-	-	-
Yes	1.44 (1.12 – 1.86)*	0.99 (0.83 – 1.13)	1.18 (1.02 – 1.38)*
Survey year			
2005 (Ref)	-	-	-
2006	1.01 (0.71 – 1.43)	1.42 (1.14 – 1.78)*	1.09 (0.91 – 1.31)
2007	1.15 (0.83 – 1.59)	1.42 (1.15 – 1.75)*	1.03 (0.85 – 1.24)
2008	1.43 (1.08 – 1.88)*	0.95 (0.73 – 1.25)	0.84 (0.68 – 1.04)
2009	0.74 (0.48 – 1.14)	0.97 (0.72 – 1.31)	0.77 (0.57 – 1.03)
Race/Ethnicity			
White Non-Hispanics	-	-	-
Black Non-Hispanics	1.06 (0.70 – 1.62)	0.70 (0.50 – 0.98)*	0.99 (0.69 – 1.43)
Hispanics	0.85 (0.40 – 1.84)	1.10 (0.67 – 1.78)	0.69 (0.45 – 1.08)
Other	1.15 (0.47 – 2.81)	1.17 (0.64 – 2.15)	1.05 (0.69 – 1.61)
Age in years			
65 – 69 (Ref)	-	-	-
70 – 74	1.41 (0.93 – 2.14)	1.31 (0.99 – 1.73)	1.05 (0.80 – 1.39)
75 – 79	1.92 (1.25 – 2.96)*	1.58 (1.18 – 2.10)*	1.22 (0.93 – 1.61)
80 – 84	1.36 (0.84 – 2.20)	1.54 (1.11 – 2.13)*	1.08 (0.80 – 1.45)
85+	1.92 (1.21 – 3.05)*	1.54 (1.13 – 2.11)*	1.11 (0.83 – 1.50)

Table 4 (Continued). Multivariate analysis of determinants of depression in elderly Medicare beneficiaries stratified by number of comorbidities

	Number of comorbidities		
	None, n = 2, 790	1, n = 4, 028	>= 2, n = 3, 247
Variables	ARR (95% C.I)	ARR (95% C.I)	ARR (95% C.I)
Marital status			
Married (Ref)	-	-	-
Widowed	1.55 (1.12 – 2.15)*	1.68 (1.32 – 2.14)*	1.33 (1.08 – 1.65)*
Divorced/separated	1.41 (0.96 – 2.08)	1.40 (1.05 – 1.85)*	1.18 (0.90 – 1.55)
Other	0.66 (0.32 – 1.39)	0.77 (0.40 – 1.46)	1.45 (0.78 – 2.71)
Education			
Less than high school (Ref)	-	-	-
High school	0.77 (0.58 – 1.03)	0.84 (0.68 – 1.04)	0.74 (0.60 – 0.91)*
College	0.68 (0.49 – 0.96)*	0.67 (0.52 – 0.87)*	0.69 (0.57 – 0.85)*
Income level			
Less than $15,000 (Ref)	-	-	-
$15,000 - $25, 000	0.73 (0.47 – 1.12)	1.08 (0.80 – 1.45)	1.03 (0.76 – 1.36)
More than $25, 000	0.59 (0.38 – 0.91)*	0.81 (0.59 – 1.11)	0.70 (0.51 – 0.92)*
Insurance coverage			
Medicare only (Ref)	-	-	-
ESI[a]	1.04 (0.75 – 1.45)	1.03 (0.83 – 1.27)	0.99 (0.82 – 1.20)
SP[b]	1.20 (0.86 – 1.66)	0.73 (0.58 – 0.93)*	1.01 (0.80 – 1.26)
ESI and SP[c]	0.96 (0.52 – 1.78)	1.12 (0.79 – 1.60)	0.81 (0.56 – 1.17)

[a] Employer Sponsored Insurance (ESI) and Medicare
[b] Self-purchased (SP) insurance and Medicare
[c] Employer sponsored, self-purchased and Medicare insurance
*Significant at p –value < 0.05

We stratified our analysis into types of comorbidity strata as shown in table 5. In particular, the risk of depression due to BPH was substantially higher among those with cancer (ARR, 1.34; 95% CI, 1.10-1.64) and heart disease (ARR, 1.15; 95% CI, 1.02-1.31).

Table 6 shows results of our multivariate analysis by survey year. Except for the year 2006, there was a consistent higher risk of depression men with BPH compared to those with no BPH, however only year 2008 was significant.

Results from our subset analysis of the association between BPH and depression based on claims data only showed estimates for the prevalence of depression at 3% and

BPH at 22%. In contrast, the prevalence of depression based on survey data was 10% and for BPH was 26%. The risk of depression was significantly higher among those with clinically diagnosed BPH compared no BPH (ARR, 1.78; 95% CI, 1.36-2.33). Although, the risk of self-reported depression was higher among self-reported BPH compared with no BPH, it was not statistically significant (ARR, 1.06; 95% CI, 0.93-1.21). Another important observation of the subset analysis was that individuals who had additional private insurance coverage (such as self-purchased and employer sponsored insurance) compared to those with Medicare only had a higher risk of clinically diagnosed depression. On the contrary, the risk of self-reported depression was significantly lower among those who had additional insurance compared with Medicare only insurance.

Table 5. Multivariate analysis of determinants of depression in elderly Medicare beneficiaries stratified by type of comorbidities.

Variables	Cancer ARR[a] (95% C.I) n = 3,218	Diabetes ARR (95% C.I) n = 2,732	Arthritis ARR (95% C.I) n = 472	Heart disease ARR (95% C.I) n = 5,788	Mental Health ARR (95% C.I) n = 1,033
Benign prostatic hyperplasia					
No (Ref)	-	-	-	-	-
Yes	1.34 (1.10 – 1.63)	1.15 (0.96 – 1.38)	1.28 (0.87 – 1.88)	1.15 (1.02 – 1.31)	1.09 (0.96 – 1.24)
Survey year					
2005 (Ref)	-	-	-	-	-
2006	1.24 (0.97 – 1.57)	1.19 (0.93 – 1.52)	1.01 (0.64 – 1.60)	1.23 (1.05 – 1.44)	1.02 (0.86 – 1.21)
2007	1.29 (1.05 – 1.59)	1.17 (0.91 – 1.50)	1.21 (0.79 – 1.86)	1.26 (1.07 – 1.47)	1.18 (1.01 – 1.39)
2008	1.08 (0.85 – 1.38)	0.97 (0.74 – 1.27)	1.23 (0.73 – 2.09)	0.92 (0.76 – 1.12)	1.01 (0.82 – 1.25)
2009	0.94 (0.66 – 1.35)	0.84 (0.58 – 1.21)	1.22 (0.55 – 2.74)	0.91 (0.71 – 1.17)	1.27 (0.80 – 2.02)
Race/Ethnicity					
White Non-Hispanics (Ref)	-	-	-	-	-
Black Non-Hispanics	1.58 (0.89 – 2.82)	0.72 (0.51 – 1.10)	0.73 (0.30 – 1.78)	0.79 (0.60 – 1.05)	1.09 (0.82 – 1.46)
Hispanics	0.65 (0.28 – 1.53)	0.69 (0.44 – 1.08)	2.08 (1.05 – 4.12)	0.84 (0.56 – 1.24)	1.12 (0.78 – 1.60)
Other	1.19 (0.62 – 2.29)	0.73 (0.42 – 1.24)	1.65 (0.79 – 3.47)	1.07 (0.73 – 1.56)	1.08 (0.68 – 1.72)
Age in years					
65 – 69 (Ref)	-	-	-	-	-
70 – 74	1.84 (1.18 – 2.87)	1.10 (0.82 – 1.48)	0.89 (0.52 – 1.53)	1.02 (0.81 – 1.29)	1.13 (0.90 – 1.44)
75 – 79	2.14 (1.41 – 3.25)	1.21 (0.90 – 1.65)	0.77 (0.46 – 1.32)	1.24 (0.99 – 1.55)	1.24 (0.99 – 1.55)
80 – 84	1.86 (1.19 – 2.90)	1.19 (0.86 – 1.65)	0.77 (0.46 – 1.30)	1.13 (0.88 – 1.44)	1.05 (0.82 – 1.34)
85+	2.00 (1.31 – 3.05)	1.07 (0.76 – 1.49)	0.73 (0.40 – 1.33)	1.08 (0.8 – 1.37)	1.16 (0.90 – 1.49)

Table 5 (Continued). Multivariate analysis of determinants of depression in elderly Medicare beneficiaries stratified by type of comorbidities

Variables	Cancer ARR[a] (95% C.I) n = 3,218	Diabetes ARR (95% C.I) n = 2,732	Arthritis ARR (95% C.I) n = 472	Heart disease ARR (95% C.I) n = 5,788	Mental Health ARR (95% C.I) n = 1,033
Marital status					
Married (Ref)	-	-	-	-	-
Widowed	1.43 (1.17 – 1.76)	1.53 (1.18 – 1.99)	1.23 (0.76 – 1.99)	1.51 (1.29 – 1.77)	1.10 (0.94 – 1.28)
Divorced/separated	1.15 (0.86 – 1.54)	1.38 (1.03 – 1.84)	0.83 (0.44 – 1.58)	1.24 (0.99 – 1.54)	0.99 (0.79 – 1.23)
Other	1.02 (0.59 – 1.78)	1.52 (0.69 – 3.36)	1.63 (0.64 – 4.17)	1.30 (0.71 – 2.39)	1.22 (0.85 – 1.76)
Education					
Less than high school (Ref)	-	-	-	-	-
High school	0.76 (0.61 – 0.95)	0.77 (0.58 – 1.02)	0.81 (0.53 – 1.25)	0.76 (0.64 – 0.90)	0.97 (0.82 – 1.15)
College	0.58 (0.46 – 0.73)	0.76 (0.60 – 0.98)	0.78 (0.49 – 1.23)	0.69 (0.58 – 0.82)	0.92 (0.79 – 1.06)
Income level					
Less than $15,000 (Ref)	-	-	-	-	-
$15,000 - $25, 000	0.83 (0.61 – 1.13)	0.89 (0.65 – 1.21)	1.94 (0.83 – 4.56)	1.05 (0.83 – 1.33)	1.17 (0.90 – 1.51)
More than $25, 000	0.57 (0.42 – 0.77)	0.62 (0.44 – 0.88)	1.32 (0.56 – 3.13)	0.79 (0.62 – 1.01)	1.04 (0.79 – 1.38)
Insurance coverage					
Medicare only (Ref)	-	-	-	-	-
ESI[b]	1.07 (0.87 – 1.30)	0.99 (0.78 – 1.26)	1.19 (0.72 – 1.96)	1.01 (0.86 – 1.19)	0.99 (0.84 – 1.16)
SP[c]	0.92 (0.73 – 1.15)	0.93 (0.72 – 1.22)	1.24 (0.77 – 2.00)	0.93 (0.71 – 1.13)	1.00 (0.83 – 1.20)
ESI and SP[d]	0.92 (0.66 – 1.30)	1.19 (0.75 – 1.87)	1.12 (0.47 – 2.87)	0.88 (0.65 – 1.19)	0.84 (0.62 – 1.13)

[a] Adjusted risk ratio
[b] Employer Sponsored Insurance (ESI) and Medicare
[c] Self-purchased (SP) insurance and Medicare
[d] Employer sponsored, self-purchased and Medicare insurance

Table 6. Multivariate analysis of determinants of depression in elderly Medicare beneficiaries stratified by survey year.

Variable	2005 ARR* (95% C.I) n = 3,913	2006 ARR* (95% C.I) n = 3,894	2007 ARR* (95% C.I) n = 3,994	2008 ARR* (95% C.I) n = 3,967	2009 ARR* (95% C.I) n = 3,667
Benign prostatic hyperplasia					
No (Ref)	-	-	-	-	-
Yes	1.13 (0.89 – 1.43)	0.88 (0.73 – 1.06)	1.08 (0.86 – 1.36)	1.40 (1.11 – 1.75)	1.18 (0.92 – 1.50)
Total Comorbidities					
0 (Ref)	-	-	-	-	-
1	1.30 (0.99 – 1.71)	1.36 (0.99 – 1.88)	1.45 (1.02 – 2.07)	1.22 (0.87 – 1.72)	1.53 (1.12 – 2.07)
2 or more	2.37 (1.82 – 3.07)	2.90 (2.18 – 3.87)	3.35 (2.43 – 4.60)	2.42 (1.81 – 3.25)	1.80 (1.32 – 2.45)

*Adjusted relative risk and 95% confidence intervals for the relation between depression and BPH stratified by survey years and adjusted for age group, race, marital status, education, income level, insurance coverage and number of comorbidities.

Discussion

Our study used population based longitudinal data of elderly men aged 65 years or above and were enrolled in the Medicare program from 2005 through 2009, to examine the co-occurrence of depression and BPH. The present study showed that depression is a common problem among elderly men 65 years or above in the United States. Overall, the risk of depression is 16% higher among elderly men with BPH. Even with possible under-diagnosis of clinical depression in elderly men, there is a significant relation between clinically diagnosed depression and BPH.

Studies of the relation between depression and BPH in men have generally shown a significant positive effect of BPH [108, 125, 126, 128, 129]. We also found that the association of depression in late life and BPH was two folds higher among elderly men with two or more comorbidities such as heart diseases, diabetes mellitus, and cancers excluding prostrate and skin cancers. This finding is also consistent with other studies that have reported significant relations between chronic medical conditions like cancer, diabetes, and cardiovascular diseases, and depression in the elderly population [3, 4, 12, 48, 158-161]. Notably, our study approach allows us to control for the confounding effect of these comorbidities on the relation of depression and BPH in the elderly men.

Findings from our study also suggest an increasing proportion of aging elderly male Medicare beneficiaries, especially those 85 years or above. This supports the reports about increasing population of the elderly in the US [3, 4, 12, 48, 158-162]. Furthermore, we found that increasing age is associated with higher risk of depression in men. Aging process is a predisposing risk for of multiple medical morbidities [141]. The strong association between depressions with age 85 or above compared to those between ages

65 and 69, may suggest deteriorating health status and the quality of life of the very old male population. Other studies suggest that delayed recognition or treatments of depression are significantly associated with increased morbidity, worsening medical conditions and poor quality of life among the elderly [141, 163, 164].

The findings from the present study also revealed that socio-demographic factors including marital status, income level, education level and health insurance coverage might influence occurrence of depression in this population. A higher risk of depression was found in elderly widowed and divorced/separated men compared with married men. The effect of marital status and depression in elderly population has also been reported in other studies [4, 135, 165-167]. Therefore, strategies to provide an effective social support system are critical to reduce further disability from depression and to improve the quality of life among aging men especially for the very old and socially isolated. Our study also supports the findings from other studies on effect of higher education and income levels on lower risk of depression [166, 168]. Higher income and education level probably provides better access to information and affordable health care. One interesting finding from this study was that the risk of clinically diagnosed depression was higher among elderly men with Medicare with additional private insurance (such as self-purchased and employer-sponsored insurance). This suggests that additional insurance may allow patients visit physicians more often and be diagnosed depression. In contrast, the risk of self-reported depression is lower in elderly men who have both Medicare plus additional private insurance compared with Medicare only insurance. This is not contradicting to the findings for clinical depression because self-report depression refers to any depressive symptoms of which some are moderate and do not fit for clinical

diagnosis. It is likely that people with better health insurance will be better taken care of thus less likely to report depression. These findings may inform further research on influence of socioeconomic disadvantage and depression in elderly men with BPH.

This study has several strengths. First, it is a community based national representative sample of US aging men. Second, we considered the effects of significant comorbidities such as cancer, heart diseases and arthritis in the elderly population. Third and more importantly, we defined depression and BPH using both clinically defined ICD-9 CM codes in the physicians' claim data and self-report in MCBS health survey data. This allows us to address depression more accurately. Finally, we considered other important socio-demographic characteristics associated with depression during our analysis, which minimizes the effect of confounding by these characteristics. Some of the study's limitations include a cross-sectional design when data analyzed by year, so we could not assess causality. The validity of the instrument used to assess depression is unknown. Therefore, using the self-report data to define depression might not be reliable.

Conclusion

This study shows that depression is prevalent among elderly male population in the US. Consistent with other studies, we observed that the prevalence of depression and benign prostatic hyperplasia (BPH) are high in elderly men. BPH is significantly related to a higher risk of depression in this population. This risk of depression is further increased by the presence of other medical conditions like cancer, diabetes mellitus, and heart diseases. The association is further strengthened between clinically diagnosed depression and BPH in elderly men. In addition, our results support the importance of socioeconomic factors such as marital status, education and income levels on the risk of

depression in the elderly. Therefore, evaluating elderly men with BPH for depression symptoms in healthcare facilities is critical to reduce further disability and to improve the quality of life.

CHAPTER 3

ESTIMATING THE TRANSITION PROBABILITY OF DEPRESSION IN ELDERLY MEN WITH BENIGN PROSTATIC HYPERPLASIA

Introduction

Benign prostatic hyperplasia (BPH) is a common non-cancerous enlargement of the prostate gland in aging men. The prevalence ranges from 20% to 60% in men ages 65 years or above [98, 101, 111, 169, 170]. Common lower urinary tract symptoms (LUTS) include increased urinary frequency, urgency, nocturnal urination, weak urinary stream and incomplete bladder emptying. The LUTS is a burdensome symptom complex with significantly negative impact on the quality of life among elderly men [105, 126, 127, 171]. The LUTS worsens over time if no appropriate treatment is provided. While the management of BPH continues to evolve rapidly, surgical treatments including minimally invasive surgical treatments, remain the mainstay for preventing disease progression [110]. Although the risk of BPH is higher with increasing age, the pathological mechanism of BPH is still not clear. Studies have hypothesized inflammatory process and hormonal pathways as the most probable mechanisms through which BPH develops [108, 172, 173]. It has been suggested that high levels of active metabolite dihydrotestosterone (DHT) and androgen receptors (AR) are major hormonal factors [122, 123, 174, 175].

Studies have shown poorer emotional outcomes and decreased quality of life in elderly men with LUTS [17, 176-178], however, only a few studies have evaluated the relationship between depression and BPH in aging men. Results from recent studies, including our previous study, suggest an increased risk of depression in men with BPH [108, 125-129]. The time order between depression and BPH is not quite understood.

Huang et al, 2011, employed survival analysis strategy to examine the induction time of depression in men with BPH. They observed that the risk of depression increased within one year of developing BPH symptoms [125]. However, the interpretation of this result is limited due the weakness of the survival analysis in this study. For example, information about depression and BPH would have been missing as result of censoring participants. Given the importance of BPH as a risk of late life depression in elderly men, there is a need to examine how the change of BPH status may influence depression status and to elucidate the time order of disease progression.

The aim of this study is to evaluate the relationship of different depression and BPH status in elderly men, using the Markov transition modeling approach. The Markov transition modeling is a natural model of repeated categorical outcome [179]. It is used frequently to investigate the natural history of chronic diseases and to predict the long-term benefits of intervention [134, 180-183].

The Markovian transition assumes that patients are always in one of a finite number of states of health, thus providing a convenient way of modeling prognosis for clinical problems with ongoing risk change [179, 181, 182, 184, 185]. For the purpose of our study, we used a longitudinal data drawn from the Medicare Current Beneficiary Survey (MCBS) and the claims data to examine the transition risk of depression status in elderly men with different BPH status.

Materials and methods

Study design

Briefly, the Medicare Current Beneficiary Survey (MCBS) is a rotating panel survey of a national representative sample of Medicare beneficiaries [186]. It provides

longitudinal data on health status, Medicare utilization, prescription drug use and expenditures. The current study used longitudinal data collected from interview rounds 37, 40, 43, 46, and 49 of the MCBS during the fall of 2005 through fall of 2009. Sampled persons who are living in the community will yield longitudinal series of data on the use of health services, medical care expenditures, health insurance coverage. Our final study population was elderly men aged 65 years or above who had at least one year follow up and were free from prostate cancer. We constructed the transition time based on the follow up years. This study followed 5,807 elderly men from the baseline to the first follow up year to construct the first transition, and 3,138 subjects from the first follow up year to the second follow up year as the second transition time.

Outcome measure

Depression: The MCBS has two questions about depression in the survey questionnaire: (1) if respondent was sad or depressed in the past 12 months ("all of the time", "most of the time", "some of the time", "a little of the time" and "none of the time". (2) If respondent had loss of interest in the past 12 months ('yes" or "no"). We defined depression as follows: (1) Any respondent who reported sad or depressed "all of the time" or "most of the time"; (2) sad or depressed "some of the time" and also loss of interest. (3) Clinical cases of depression from the Medicare claim's data using the International Classification of Disease, ninth edition Clinical Modification (ICD-9-CM) codes. Depression codes include 296.2 (major depressive disorder, single episodes), 296.3 (major depressive disorder, recurrent episodes), 300.4 (neurotic depression), 309.0 (Adjustment disorder with depressed mood), 309.1 (prolonged depressive reaction), and 311 (depression, not elsewhere classified).

Independent variable

Respondents with BPH were identified from the response to the MCBS survey question on whether past year respondent was told he had enlarged prostate/BPH ("yes"/"no"). The second measure of BPH was from the ICD-9-CM codes reported in the claims data. The ICD-9-CM codes according to Urologic disease in America's recommendation were 594.1 (Other calculus in bladder), 599.6 (Urinary obstruction), 599.60 (Urinary obstruction, unspecified), 600 (hyperplasia of the prostrate), 788.2 (Retention of urine), and 788.4 (Frequency of urination and polyuria) [101]. The two sources were combined to define BPH in this study.

Covariates

Other information collected includes socio-demographic characteristics (age group, education, race, income, marital), insurance coverage and medical condition such as heart diseases, arthritis, diabetes mellitus, mental health conditions and cancer (excluding skin cancer). Comorbidities were categorized as yes or no based on the response to whether in the past year a doctor ever told them they had any of the above medical conditions. Age groups include 65 – 69, 70 – 74, 75 – 79, 80 – 84 and 85+. We categorized race into White, Black, Hispanics and others (American Indian, Asian or Pacific Islander, etc.). Other variables included in our analysis were marital status (married, widowed, divorced/separated, and other), education (Less than high school, High school and College certificates), income level (Less than $15,000, $15,001 - $25, 000, and more than $25, 000), and insurance coverage (Medicare only, Both Medicare and Employer-sponsored insurance (ESI), Both Medicare and Self-purchased).

Defining Markov state

The Markov transition model is a stochastic modeling process [187, 188]. The Markov process refers to subjects in a hypothetical cohort with a health condition moving between different health states over time (time dependent Markov process) [189]. We divided depression and BPH into distinctive and mutually exclusive states and assigned transition probabilities for moving between states over a period. The Markov process for depression were: no-depression in both years, moving from no-depression state in previous year to depression in current year, depression in previous year to no-depression in current year, and persistent depression for both years (Figure 1). Similarly, we defined BPH Markov processes as no-BPH in both years, move from no-BPH state in previous year to BPH in current year, move from BPH in previous year to no-BPH in current year, and persistent BPH for both years (Figure 2).

Factors that could influence the transitions states include patients receiving any treatment for depression or BPH (surgical or medical treatment for BPH) during the study period, adherence to treatment, duration of treatment and other unknown factors.

Transition times

The first transition time was from baseline to the first follow up year, and the second transition started from the end of first transition to the second year of follow-up. In total, the subjects were followed for two years.

		Depression time 2	
		-	+
Depression time 1	-	No depression in both years (Tpd1)	No depression to depression (Tpd2)
	+	Depression to no depression (Tpd3)	Persistent depression (Tpd4)

Tpd1 = transition probability no depression in both years
Tpd2 = transition probability from no depression to depression
Tpd3 = transition probability from depression to no depression
Tpd4 = transition probability of persistent

Figure 1. Markov process for depression progression.

		BPH time 2	
		-	+
BPH time 1	-	No BPH in both years (Tpb1)	No BPH to BPH (Tpb2)
	+	BPH to no BPH (Tpb3)	persistent BPH (Tpb4)

Tpb1 = transition probability no BPH in both years
Tpb2 = transition probability from no BPH to BPH
Tpb3 = transition probability from BPH to no BPH
Tpb4 = transition probability persistent BPH

Figure 2. Markov process for BPH progression.

Statistical analysis

We linked MCBS interview data with the Medicare claims from 2005 to 2009 using the base identification numbers. Our analysis was restricted to community dwelling elderly men ages 65 years or above and also being followed up for at least one year. The following were excluded hierarchically from our analysis: cases with prostate cancer (n=133) and end-stage renal disease (n = 5). Descriptive statistics were performed for the overall study population at the baseline using the SURVEYFREQ procedure in SAS. The

proportions of Markov health states for depression and BPH by transition times were estimated.

Generalized linear mixed models were used to estimate the instantaneous likelihood of transition (Adjusted transition rates (ATR)), with covariance matrix estimated by generalized estimating equations to explain the variation between repeated measures (PROC GENMOD in SAS). We accounted for the complex sampling design by incorporating the multilevel clusters and survey weight variables into all the analysis. All analyses was done using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

At baseline, there were 5,807 elderly male beneficiaries who were eligible for the study and followed for at least one year to determine the first transition probabilities. Of them, 54% (n= 3138) were followed up for another year to determine the second transition probabilities. The summary of baseline characteristics of the participants is shown in table 7. The median age was 71. Nearly 9% (n=518) were depressed and 37% had BPH at the start of the study. White males (88%) and married men (73%) were majority in the study population.

Table 7. Baseline summary of characteristics of study sample before transition.

Variables	N = 5, 807	Weighted percentage
Depressed		
No	5, 289	91.4
Yes	518	8.6
Benign prostatic hyperplasia		
No	3, 615	63.5
Yes	2, 192	36.5
Race/Ethnicity		
White Non-Hispanics	5, 135	88.1
Black Non-Hispanics	393	7.2
Hispanics	125	1.9
Other	154	2.8
Age in years		
65 – 69	1, 534	31.8
70 – 74	1, 251	23.4
75 – 79	1, 260	21.7
80 – 84	1, 0.95	14.6
85+	667	8.4
Marital status		
Married	4, 204	73.3
Widowed	917	14.1
Divorced/separated	518	9.6
Other	168	3.1
Education		
Less than high school	1, 539	25.0
High school	1, 863	32.5
College	2, 405	42.6
Income level		
Less than $15,000	463	7.6
$15,000 - $25, 000	1, 852	30.4
More than $25, 000	3, 492	62.0
Comorbidity		
Diabetes	1, 397	23.9
Arthritis	157	2.6
Cancer	1, 647	26.8
Heart disease	2, 949	50.3
Mental Health[μ]	477	8.1

Table 7 (Continued). Baseline summary of characteristics of study sample before transition.

Variables	N = 5, 807	Weighted percentage
Insurance coverage		
Medicare only	1, 941	33.8
ESI[a]	2, 028	35.0
SP[b]	1, 381	23.0
ESI and SP[c]	457	8.2
Total Comorbidities		
0	1, 625	29.4
1	2, 341	39.8
2 or more	1, 841	30.9

[a] Employer Sponsored Insurance (ESI) and Medicare
[b] Self-purchased (SP) insurance and Medicare
[c] Employer sponsored, self-purchased and Medicare insurance

The proportion with college education was 43% and 62% had income levels of greater than $25, 000. Heart diseases including myocardial infarction, heart valve diseases etc. are the most common medical conditions, followed by cancer. Elderly men with Medicare only insurance accounted for about 34% (n=1,941) of the study sample.

The proportion of different depression and BPH states in two-transition time points are shown in tables 8. Approximately 86% remained free of depression in the two transition times, 5% moved from non-depression to depression state, and a similar percent from depression to no depression, and about 4% had depression at both time points. In addition, about 51% remained in no BPH health state for both time points and 11-12% moved from no BPH to BPH state, and 12% from BPH to no BPH and about 26% had BPH in both time points (Table 8).

Table 8. Summary of BPH and depression status by Transition time points

	Transition time	
	1	2
	N=5, 807	N= 3, 138
Variables	n (%)	n (%)
Depression states[a]		
No depression in both years	4, 968 (85.8)	2, 708 (86.7)
No depression to depression	321 (5.5)	171 (5.3)
Depression to no depression	293 (5.1)	142 (4.3)
Persistent depression	225 (3.7)	117 (3.7)
Benign prostatic hyperplasia states[b]		
No BPH in both years	2, 894 (50.7)	1, 555 (50.7)
No BPH to BPH	721 (12.1)	341 (10.7)
BPH to no BPH	698 (11.6)	376 (11.9)
Persistent BPH	1514 (25.5)	866 (26.7)

[a]Depression Markov states
[b]Benign prostatic hyperplasia (BPH) Markov states

Transition probability matrix for the relation of depression and BPH is summarized in table 9. At the first transition time, 87% of men who remained no BPH health status also were in no depression state, while 5% of them moved in to depression status. In contrast, 5.8% of those who moved from no BPH in previous year to BPH in current year also moved from no depression to depression. Among those who moved from BPH in previous year to no BPH, 6.7% also moved from depression to no depression (Table 9). Results of the second transition matrix are similar. The proportion persons who moved from no BPH to BPH state had about 6% chances of transiting from no-depression to depression state.

Table 9. Transition probability matrix for depression and benign prostatic hyperplasia (BPH) relation

	Depression states			
	No depression in both years	No depression to depression	Depression to no depression	Persistent depression
First transition time (N=5, 807)				
BPH[a] states	n (%)	n (%)	n (%)	n (%)
No BPH in both years	2, 516 (87.2)	158 (5.3)	128 (4.4)	92 (3.1)
No BPH to BPH	599 (83.5)	44 (5.8)	39 (5.3)	39 (5.3)
BPH to no BPH	582 (85.5)	30 (4.8)	45 (6.7)	21 (3.0)
Persistent BPH	1, 271 (84.1)	89 (5.8)	81 (5.5)	73 (4.6)
Second transition time (N = 3, 138)				
No BPH in both years	1, 356 (87.6)	83 (5.1)	66 (4.0)	50 (3.3)
No BPH to BPH	298 (86.6)	20 (6.8)	12 (3.5)	11 (3.1)
BPH to no BPH	315 (83.8)	23 (6.0)	18 (4.7)	20 (5.5)
Persistent BPH	739 (86.4)	45 (4.9)	46 (4.8)	36 (3.9)

[a]Benign prostatic hyperplasia

Results from the multivariate analysis (Table 10) show that depression transition status is generally consistent with BPH transition status. In particular, the likelihood of moving from BPH to no BPH is significantly associated with moving from depression to no depression than remaining in no-depression state (ATR, 1.49; 95% CI, 1.05-2.12;p-value = 0.025). For those with persistent BPH, the transition probabilities of depression appears independent of BPH status, and persistent depression also appears independent of BPH status. The other significant factors that influenced the transition states of depression in elderly men were age group, marital status, education and number of comorbidities. We found that being a widower compared to being married significantly changes depression status. Age groups of 70 years and above compared to 65 to 69 are less likely to affect the transition processes of depression. In addition, the transition of depression is lower in those with education levels of high school and above compared to

less than high school, and income levels of more than $ 25, 000 compared to less than $25, 000. Having two or more comorbidities compared to no comorbidity increased the rate of transition from no depression to depression by about two fold (ATR, 2.16; 95% CI 1.67-2.81; p-value=0.021) and to persistent depression by 2.5 fold (ATR, 2.55; 95% CI, 1.78-3.66; p-value < 0.0001). Similar findings were observed in the analysis of the second transition time but no significant association was found between BPH status and depression status (Table 11).

Table 10. Estimation of forward and backwards rates for depression in the first transition time: Results from multivariate models

	Depression state[a]		
Variables	**No depression to depression** ATR[b] (95% CI)	**Depression to no depression** ATR (95% CI)	**Persistent depression** ATR (95% CI)
BPH[c] states			
No BPH in both years (Ref)	-	-	-
No BPH to BPH	1.03 (0.74 – 1.44)	1.26 (0.88 – 1.82)	1.63 (1.12 – 2.38)
BPH to no BPH	0.93 (0.62 – 1.39)	1.49 (1.05 – 2.12)	1.05 (0.65 – 1.68)
Persistent BPH	1.15 (0.88 – 1.51)	1.37 (1.02 – 1.83)	1.52 (1.11 – 2.09)
Race/Ethnicity			
White Non-Hispanics (Ref)	-	-	-
Black Non-Hispanics	0.91 (0.59 – 1.41)	0.98 (0.62 – 1.55)	0.71 (0.42 – 1.18)
Hispanics	1.29 (0.71 – 2.34)	1.39 (0.74 – 2.62)	1.16 (0.53 – 2.57)
Other	0.82 (0.39 – 1.74)	1.03 (0.48 – 2.19)	0.52 (0.19 – 1.40)
Age in years			
65 – 69 (Ref)	-	-	-
70 – 74	0.63 (0.45 – 0.89)	0.86 (0.60 – 1.22)	0.59 (0.40 – 0.90)
75 – 79	0.98 (0.71 – 1.36)	1.03 (0.72 – 1.48)	0.74 (0.50 – 1.10)
80 – 84	0.75 (0.52 – 1.07)	0.73 (0.50 – 1.08)	0.59 (0.39 – 0.91)
85+	0.91 (0.62 – 1.34)	0.86 (0.56 – 1.32)	0.87 (0.57 – 1.33)
Marital status			
Married (Ref)	-	-	-
Widowed	1.46 (1.10 – 1.95)	1.71 (1.26 – 2.33)	1.77 (1.29 – 2.43)
Divorced/separated	1.40 (0.99 – 1.99)	1.94 (1.37 – 2.74)	1.18 (0.76 – 1.81)
Other	0.47 (0.18 – 1.23)	0.87 (0.40 – 1.88)	1.42 (0.70 – 2.86)
Education			
Less than high school (Ref)	-	-	-
High school	0.77 (0.59 – 1.02)	0.94 (0.70 – 1.26)	0.74 (0.53 – 1.01)
College	0.80 (0.60 – 1.06)	0.76 (0.55 – 1.05)	0.64 (0.45 – 0.89)
Income level			
Less than $15,000 (Ref)	-	-	-
$15,000 - $25, 000	1.06 (0.71 – 1.57)	1.03 (0.68 – 1.56)	0.92 (0.59 – 1.43)
More than $25, 000	0.60 (0.40 – 0.92)	0.68 (0.44 – 1.07)	0.53 (0.33 – 0.86)

Table 10 (Continued). Estimation of forward and backwards rates for depression in the first transition time: Results from multivariate models.

	Depression state[a]		
Variables	**No depression to depression** ATR[b] (95% CI)	**Depression to no depression** ATR (95% CI)	**Persistent depression** ATR (95% CI)
Insurance coverage			
Medicare only (Ref)	-	-	-
ESI[d]	1.07 (0.82 – 1.40)	1.13 (0.84 – 1.54)	1.03 (0.74 – 1.45)
SP[e]	0.88 (0.65 – 1.21)	0.99 (0.72 – 1.37)	1.11 (0.78 – 1.57)
ESI and SP[f]	1.44 (0.96 – 2.18)	1.27 (0.79 – 2.06)	0.91 (0.49 – 1.67)
Total Comorbidities			
0 (Ref)	-	-	-
1	1.27 (0.93 – 1.74)	0.94 (0.69 – 1.28)	0.94 (0.63 – 1.42)
2 or more	2.22 (1.64 – 3.00)	1.42 (1.06 – 1.91)	2.55 (1.78 – 3.66)

[a]Depression states: Ref = 0 (No depression in both years)
[b]Adjusted transition rate
[c]Benign prostatic hyperplasia
[d] Employer Sponsored Insurance (ESI) and Medicare
[e] Self-purchased (SP) insurance and Medicare
[f]Employer sponsored, self-purchased and Medicare insurance

Table 11: Estimation of forward and backwards rates for depression in the second transition time: Results from multivariate models.

	Depression state[a]		
Variables	**No depression to depression** ATR[b] (95% CI)	**Depression to no depression** ATR (95% CI)	**Persistent depression** ATR (95% CI)
BPH[c] states			
No BPH in both years (Ref)	-	-	-
No BPH to BPH	1.25 (0.76 – 2.04)	0.94 (0.53 – 1.67)	1.10 (0.59 – 2.03)
BPH to no BPH	1.20 (0.76 – 1.89)	1.30 (0.79 – 2.16)	1.78 (0.58 – 2.98)
Persistent BPH	0.95 (0.67 – 1.36)	1.14 (0.78 – 1.65)	1.31 (0.86 – 2.01)

[a]Depression states: Ref = 0 (No depression in both years)
[b]Adjusted transition rate
[c]Benign prostatic hyperplasia

Discussion

The present study used data from a dynamic cohort of a nationally representative sample of elderly men in the US to explore the transition probabilities of depression and BPH in elderly male Medicare beneficiaries. We examined depression and BPH status in two transition times over two follow up years. This is the first study that examined the progression of depression and BPH in elderly men using the time dependent Markov model. The Markov modeling technique is a natural modeling process with minimal assumptions. This is the most important strength of our study. The main advantages of using the transitional model, compared with other traditional model such as logistic regression and survival analysis, are that it allows the flexibility to explore all possible combinations of outcomes/exposures changing status, which is not possible in the traditional modeling.

A second strength of our study is that our study population was drawn from a National representative sample of the US elderly population using linked data from

MCBS health survey and Medicare claims. Thirdly, the time order in our study provides opportunities to assess cause and effect in the relation of BPH and depression.

Our results show that BPH status significantly influences the progression of depression in elderly men. For instance, our results show that moving from BPH to no-BPH significantly increases the transition rate from depressed to non-depressed states in elderly men, and having persistent BPH compared remaining with no-BPH health condition is associated with about 40% increased risk of moving to persistent depression than remaining is no-depression state. Huang et al, (2011) used survival analysis to examine the risk of depression in men with BPH compared to those with no BPH after one year follow up. Their results suggest that having BPH compared to the no BPH increased the risk of developing depression in one year among elderly Chinese population [125]. Similarly, the results from our study show that moving from no-BPH to BPH health state increases the transition rate from no-depression to depression state though not statistically significantly. In addition, we observed that having one or more comorbidity significantly increased the risk of transiting from non-depressed to depressed state by two folds. This supports findings of significant association of depression and medical conditions such as heart diseases, cancer, and diabetes in the elderly as noted in other studies [142, 146, 160, 161, 190-196].

In addition to BPH and comorbidity, our study revealed that marital status and high education significantly influence the progression of depression in elderly men. Notably, widowed or divorced/separated elderly men compared with married are associated with increased risk of change of depression status. Bereavements or loss of loved ones are common adverse events found among aging people and have been shown

to be significantly associated with depression in the elderly. For the elderly population, marriage plays a pivotal role compared to other forms of social relationship. Studies show that married individuals are more likely to have happier, life satisfaction and lower risk of depression to non-married status [197-199]. Furthermore, it has been suggested that being married is associated with healthier mental health state in the aging population [199]. Similar to other studies, our findings revealed the importance of the protective effect of higher education levels. We observed that elderly men with high school or college level education compared with less than high school levels are less likely to transit from no-depression state to depression state. In addition, those with high school or college levels education compared with those with less than high school education are less likely to transit from non-depressed to depressed state, and less likely to remain in persistent depression state [200].

This study is not without limitations. An important limitation of Markov model is the "memoryless" of process, i.e., the probability of moving in or out is independent of the state that the patients may have experienced before entering that state [187]. Secondly, the sensitivity of depression screening instrument in the MCBS questionnaire is unknown. We combined the clinically diagnosed codes from the claim data with survey questions to minimize this problem. The third limitation of this study is that we did not control for factors such as treatments types, adherence and duration of diseases that may influence the change of either depression or BPH states. Nevertheless, this study provides critical information for future investigations on the time order between BPH and depression in both clinical and population settings.

Conclusion

This study estimates the transition probabilities of depression and BPH state changes in elderly men. Results from this study indicate that transition from BPH to non-BPH states is associated with transition from depressed to non-depressed state. Presence of two or more coexisting medical conditions increases the progression to depression by two folds. These findings suggest that prompt corrective interventions in the management of BPH in elderly men may significantly reduce the progression of depression in this population.

CHAPTER 4

EFFECTS OF RACE AND SOCIOECONOMIC DISADVANTAGE ON DEPRESSION IN ELDERLY MEN WITH BENIGN PROSTATIC HYPERPLASIA

Introduction

Previous studies suggest that social and economic differences are major factors that influence health outcomes [201-203]. Race/ethnicity and income level are two key indicators of socioeconomic disadvantage in the United States [204]. Research on chronic medical morbidities suggests significant relationships between race/ethnicity and socioeconomic status (SES), and health outcome [204-207]. Depression, like many other medical conditions, disproportionately affects populations with lower SES and minority groups [208]. A study of the US population drawn from the National Health and Nutrition Examination Survey (NHANES) demonstrates that living below poverty level increases the risk of major depressive disorder by 1.5 folds [209]. Even though minority status such as being a Hispanic or African American is not exclusively related to lower SES, the largest groups of minority citizens in the United States are found in lower SES brackets [210, 211].

The mechanisms through which ethnicity and socioeconomic status may account for the differences in health outcomes include genetic predisposition, coping skills, deprivation of resources, discrimination, unequal access to health care and quality of health care [211, 212]. Studies have proposed cumulative advantage theory as an alternative explanation for the effect of SES on health outcomes [213-216]. For instance, individuals with higher SES indices such as higher education and income level have

cumulative resources that enhance their ability to avoid chronic stressors and to live a healthier lifestyle. Higher SES including higher income level is associated with more happiness and self-confidence while lower income is associated with greater vulnerability to mental health disorder [206]. Further, lower income status has been connected with more challenging experiences and emotional distresses such as feelings of hopelessness, depression, and life dissatisfaction [211]. With the increasing aging population in the United States and elsewhere, the impact of socioeconomic disadvantage on the quality of health is a major concern [1, 217-219]. Some studies suggest that inequality in risk of mental health conditions observed in the elderly population may be due to differences in SES [220-222].

Depressive disorders account for a significant proportion of mental health illness among the elderly in the United States [223]. The association between depression and chronic medical conditions has been well studied [224-228]. Recently, some studies that examined the effect of benign prostatic hyperplasia (BPH) on depression in aging men observed a higher risk of depression in those with BPH compared to those without BPH [108, 125, 126, 128-130, 224]. BPH is benign growth of the prostate gland that develops with aging in men. It is the most common cause of bothersome lower urinary tract symptoms (LUTS) such as urinary frequency, bladder outlet obstruction, nocturnal urination, and straining elderly men [99, 229-231]. Although, results from these studies suggest a relation between BPH and depression, this finding might not be directly linked to the effect of BPH, rather the relationship may be due to heterogeneity in social and economic context of the population of men with BPH.

The objective of the study was to evaluate the influence of social and economic disadvantage on association of depression in elderly men with BPH. We hypothesized that the risk of depression is higher among the minority group with BPH compared to the White elderly men with BPH, and higher among lower income groups compared to higher income group. This study used a combined five-year data from Medicare Current Beneficiary Survey (MCBS) report and the Medicare claims data.

Materials and methods

Study population

The study population was drawn from a nationally representative sample of elderly Medicare beneficiaries who participated in the health survey from 2005 through 2009. The study sample comprised of only community dwelling elderly men aged 65 years or above, who were identified as having benign prostatic hyperplasia either reported in the MCBS survey or clinically diagnosed in the claims data using the International Classification of Diseases Ninth edition (ICD 9) codes. The MCBS data is a de-identified, continuous multipurpose survey of nationally representative sample of the Medicare population including both aged and disabled enrollees conducted by the Centers for Medicare & Medicaid Service [232].

The MCBS Cost and Use File links personal interview data and Medicare claims for each survey year longitudinally. Medicare claims data include inpatient, outpatient, and physician/supplier services claims that provide additional information on the diagnosis, procedures, and cost for all the Medicare reimbursed services for the survey year. Each Participant in the MCBS survey completed questionnaires to provide demographic information including age, race, education level, annual income, marital

status, and medical conditions including BPH, depression, cancer, arthritis, heart diseases etc. In addition, we identified clinically diagnosed cases of depression and BPH using the International Classification of Disease, 9th edition Clinical Modification (ICD-9-CM reported in the Medicare claims data. For benign prostatic hyperplasia (BPH): We identified the main independent variable (BPH) from responses to the question on whether "Past year respondent was told he had enlarged prostate/BPH" ("yes" or "no"). The ICD-9-CM codes according to Urologic disease in America's recommendation for BPH were 594.1 (Other calculus in bladder), 599.6 (Urinary obstruction), 599.60 (Urinary obstruction, unspecified), 600 (hyperplasia of the prostrate), 788.2 (Retention of urine), and 788.4 (Frequency of urination and polyuria) [233, 234].

We excluded those with history of prostate cancer and those with renal failure. The final sample included 4,578 elderly men with BPH.

Measures

Outcome Measure

Depression: The survey questionnaire had two depression questions. The first question was whether the respondent was sad or depressed in the past 12 months ("all of the time", "most of the time", "some of the time", "a little of the time" and "none of the time". The second question was whether they had loss of interest in the past 12 months ('yes" or "no"). Based on the survey responses, we defined depression using two criteria: (1) Any respondent who reported sad or depressed "all of the time" or "most of the time" and (2) sad or depressed "some of the time" and loss of interest. The third definition of depression was based on the International Classification of Disease, ninth edition Clinical Modification (ICD-9-CM) codes reported in the claims data. The depression codes, based

on prior studies, include 296.2 (major depressive disorder, single episodes), 296.3 (major depressive disorder, recurrent episodes), 300.4 (neurotic depression), 309.0 (Adjustment disorder with depressed mood), 309.1 (prolonged depressive reaction), and 311 (depression, not elsewhere classified).[79, 235] The self-reported depression and the clinically diagnosed depression were then combined. We coded depression as a binary variable (yes or no).

Socioeconomic indicators

The main socioeconomic indicators in our analysis are race and income level. Other indicators include education, marital status, and health insurance. We categorized the variables as follows: Education (Less than high school, High school and College certificates). Income level (Less than $15,000, $15,001 - $25, 000, and More than $25, 000), and Insurance coverage (Private only, Medicare only, Self-purchased (SP) and Medicare, Employer sponsored Insurance (ESI) and Medicare, and Both SP/ ESI and Medicare). Other independent variables consist of demographic characteristics (age (65 – 69, 70 – 74, 75 – 79, 80 – 84 and 85+), race (White, Black, and Hispanics), Marital status (Married, Widowed, Divorced/separated, and other).

Statistical analysis

We combined all cases of reported BPH from the MCBS survey and Medicare claims data over five years period (2005 to 2009). The period prevalence was estimated and Chi-squared test was used to compare the socioeconomic characteristics. We applied the yearly weight and multilayer cluster in all our analysis. We used the SAS SURVEYFREQ procedure to calculate the proportions and weighted percentages. The adjusted risk ratio of depression was estimated using the generalized estimation equation

(GEE) method. We selected our final model using the quasi-likelihood information criteria (QIC) fit statistics, which states that the smaller is best fit. All data processing and statistical analysis was done using the SAS software version 9.4 (SAS Inc., Cary, NC).

Results

During the five years survey period, 4,578 elderly Medicare beneficiaries reported having BPH. Of them, 727 (16%) had depression. Table 12 shows the distribution of social and economic characteristics of beneficiaries with BPH. A majority of our sample population were Whites (89%, n=4,087) and married men (72%, n = 3,300). About 46% (n = 2, 090) of the total respondents had college education level, and 2,845 (62%) had annual income level of greater than $25, 000. Approximately 74% (n= 3, 395) of the beneficiaries had either additional self-purchased insurance, employer sponsored insurance or both.

Results from our multivariate analysis of socioeconomic predictors of depression in the elderly with BPH are shown in table 13. We found no significant association of race and risk of depression in elderly with BPH. Age groups 70 years and above compared with 65 to 69 years had significantly higher risk of depression. The risk of depression was 50% higher in widowed men with BPH (ARR, 1.50; 95% CI, 1.26-1.80), and 33% higher in divorced men with BPH (ARR, 1.33; 95%CI, 1.06-1.68). In contrast, compared to less than high school, the risk of depression in men with BPH was lower in educational levels of high school (ARR, 0.87; 95% CI, 0.72-1.04) or college (ARR, 0.71; 95% CI 0.59-0.85). No significant difference in the risk of depression was seen among the types of insurance coverage.

Table 12. Distribution of social and economic characteristics of elderly men with BPH by depression status.

Variables	Depressed, N=727 n (weighted %)	Not depressed, N= 3, 821 n (weighted %)
Race/Ethnicity		
White	644 (88.2)	3, 443 (89.4)
Black	49 (7.5)	218 (6.3)
Other	34 (4.3)	160 (4.3)
Age in years		
65 – 69	92 (14.7)	640 (23.4)
70 – 74	143 (22.7)	879 (24.5)
75 – 79	178 (26.6)	790 (21.4)
80 – 84	154 (17.8)	835 (17.5)
85 +	160 (18.2)	677 (13.2)
Marital status		
Married	453 (62.4)	2, 847 (75.7)
Widowed	180 (23.3)	586 (13.5)
Divorced/ Separated	75 (10.7)	284 (7.8)
Other	19 (3.6)	104 (3.0)
Education		
Less than high school	242 (31.7)	864 (21.7)
High school	223 (31.1)	1, 132 (28.9)
College	262 (36.2)	1, 825 (49.5)
Income level		
Less than $15,000	72 (9.7)	230 (5.8)
$15,000 - $25, 000	292 (39.7)	1, 109 (28.3)
More than $25, 000	363 (50.6)	2, 482 (65.8)
Insurance coverage		
Medicare only	219 (30.3)	964 (26.2)
ESI[a]	271 (37.7)	1, 481 (38.9)
SP[b]	183 (24.6)	996 (25.2)
Both ESI and SP[c]	54 (7.4)	380 (9.7)

[a] Employer Sponsored Insurance (ESI) and Medicare
[b] Self-purchased (SP) insurance and Medicare
[c] Employer sponsored, self-purchased and Medicare insurance

Table 13. Multivariate analysis of socioeconomic determinants of depression among elderly men with benign prostatic hyperplasia.

Variables	ARR[a]	95% CI
Race/Ethnicity		
White (Ref)	-	-
Black	0.93	0.69 – 1.26
Other	0.81	0.55 – 1.18
Age in years		
65 – 69 (Ref)	-	-
70 – 74	1.34	1.01 – 1.80**
75 – 79	1.68	1.28 – 2.19**
80 – 84	1.38	1.03 – 1.85**
85 +	1.60	1.20 – 2.14**
Marital status		
Married (Ref)	-	-
Widowed	1.50	1.26 – 1.80**
Divorced/ Separated	1.33	1.06 – 1.68**
Other	1.28	0.76 – 2.16
Education		
Less than high school (Ref)	-	-
High school	0.87	0.72 – 1.04
College	0.71	0.59 – 0.85**
Income level		
Less than $15,000 (Ref)	-	-
$15,000 - $25, 000	0.87	0.68 – 1.11
More than $25, 000	0.63	0.48 – 0.83**
Insurance coverage		
Medicare only (Ref)	-	-
ESI[b]	1.09	0.91 – 1.31
SP[c]	1.00	0.81 – 1.23
Both ESI and SP[d]	0.95	0.70 –1.27

[a] Adjusted risk ratio
[b] Employer Sponsored Insurance (ESI) and Medicare
[c] Self-purchased (SP) insurance and Medicare
[d] Employer sponsored, self-purchased and Medicare insurance
** Significant level with p-value < 0.05

We further stratified the analysis by race (Table 14). The result showed that among White elderly with BPH, the risk of depression was significantly higher among the widowed compared to the married men (ARR, 1.61; 95% CI, 1.33-1.95). Compared to White men with income of less than $15,000, the risk of depression was lower among Whites with income of greater than $25,000 (ARR, 0.62; 95% CI, 0.45-0.84). Whites with college level education had lower risk of depression than those with less than high school education (ARR, 0.68; 95% CI, 0.56-0.83). Similarly, among the Blacks, those income levels of greater than $25, 000 compared with less than $15,000 had significantly lower risk of depression (ARR, 0.18; 95% CI, 0.07-0.50).

Table 14. Multivariate analysis of socioeconomic determinants of depression among elderly men with benign prostatic hyperplasia comparing White and Black races.

	White, N = 4, 087	Blacks, N = 267
Variables	ARR* (95% CI)	ARR (95% CI)
Marital status		
Married (Ref)	-	-
Widowed	1.61 (1.33 – 1.95)**	1.06 (0.60 – 1.88)
Divorced/ Separated	1.27 (0.99 – 1.64)	1.43 (0.71 – 2.90)
Other	1.30 (0.75 – 2.28)	1.23 (0.35 – 4.33)
Education		
Less than high school (Ref)	-	-
High school	0.87 (0.71 – 1.05)	1.22 (0.61 – 2.42)
College	0.68 (0.56 – 0.83)**	1.59 (0.80 – 3.19)
Income level		
Less than $15,000 (Ref)	-	-
$15,000 - $25, 000	0.83 (0.63 – 1.10)	0.55 (0.28 – 1.08)
More than $25, 000	0.62 (0.45 – 0.84)**	0.18 (0.07 – 0.50)**

Note: Model was adjusted risk ratio and 95% confidence intervals were adjusted for age group, marital status, education, income level and insurance coverage. The reference for depression is no depression
** Significant level with p-value < 0.05

Table 15 shows the adjusted risk ratio and 95% confidence intervals stratified by income level. We found that showed that elderly in Other race groups (including Hispanics) with income level of less than $15,000 compared to White group had a significantly lower risk of depression (ARR, 0.29; 95% CI, 0.12-0.71). Among elderly with income levels between $15,000 and $25,000, widowed were about 58% at higher risk of depression compared to the married with BPH (ARR, 1.58; 95% CI, 1.22-2.05), while those with college level education compared to less than high school education had significantly lower risk of depression (ARR, 0.63, 95% CI, 0.45-0.87). Widowed elderly men with BPH who had annual income of greater than $25,000 were more likely to depressed than those who were married (ARR, 1.52; 95% CI, 1.15-2.01). However, those annual income of greater than $25,000 and college level education were at lower risk of depression than those with less than high school and income of $25,000 (ARR, 0.73, 95% CI, 0.55-0.97).

Table 15. Multivariate analysis of determinants of depression in elderly men with benign prostatic hyperplasia comparing income levels.

	Income groups		
	< $15, 000	**$15, 000 - $25, 000**	**>$25, 000**
	N = 302	**N = 1, 401**	**N = 2, 845**
Variables	ARR[a] (95% CI)	ARR (95% CI)	ARR (95% CI)
Race/Ethnicity			
White (Ref)	-	-	-
Black	1.26 (0.79 – 1.99)	0.91 (0.62 – 1.33)	0.60 (0.26 – 1.35)
Other	0.29 (0.12 – 0.71)**	0.93 (0.61 – 1.42)	1.35 (0.71 – 2.56)
Marital status			
Married (Ref)	-	-	-
Widowed	1.02 (0.58 – 1.80)	1.58 (1.22 – 2.05)**	1.52 (1.15 – 2.01)**
Divorced/ Separated	1.21 (0.70 – 2.08)	1.13 (0.78 – 1.63)	1.42 (0.88 – 2.30)
Other	0.96 (0.43 – 2.15)	1.06 (0.52 – 2.17)	1.46 (0.57 – 3.72)
Education			
Less than high school (Ref)	-	-	-
High school	0.58 (0.31 – 1.11)	0.86 (0.68 – 1.09)	0.93 (0.67 – 1.29)
College	1.12 (0.67 – 1.87)	0.63 (0.45 – 0.87)**	0.73 (0.55 – 0.97)**

Note: Model was adjusted risk ratio and 95% confidence intervals were adjusted for age group, race, marital status, education, and insurance coverage. The reference for depression is no depression

** Significant level with p-value < 0.05

Discussion

This study used a combined five years from the Medicare Current Beneficiary Survey and claims data to examine the influence of social and economic heterogeneity on depression in elderly men with BPH. Overall, the prevalence of depression in elderly men with BPH was approximately 16%, which was higher than that reported among community dwelling elderly (5%) and primary care setting (10%) in the United States [4, 15, 137, 138]. The results from our study showed an association between marital status, education and income levels and the risk of depression in elderly men with BPH. This was the first study that examined the effect of socioeconomic disadvantage on depression among elderly men with BPH. Although there was no statistical evidence of effect of race on depression in men with BPH, our findings suggests that even within same racial groups there may be differential effects of social and economic factors on depression. Similar associations have been reported in other studies that considered effect of socioeconomic factors on depression within racial/ethnic strata [25, 77, 204, 205, 209, 211].

Result from our study suggest that elderly White men with BPH and high income levels had lower risk of depression compared to the those in lower income levels. Riolo et al, 2005, reported similar findings in their study population drawn from the NHANES III survey. They found a significant association between poverty and major depressive disorders among Whites respondents [77]. Our findings may be explained by stressful effects of daily living experiences of lower income groups, coupled with the bothersome and psychological distresses associated with LUTS in aging men. Drawing from the cumulative disadvantage/advantage theory, income level may be an important factor that

determines the risk of developing depression in men with BPH during late life. The theory of cumulative disadvantage highlights ways an early social and economic advantage or disadvantage may differentiate a population's health trajectory over time [214-216, 236]. Inequality in access to care is a common consequence of socioeconomic disadvantage. For instance, individuals who cannot afford adequate health insurance are faced with limited health care choices. Other studies suggest that inadequate access to healthcare, more common among person with low income and minority, was an important prognostic factor for poor health outcomes [237-241]. Further, we observed that within the high-income group, those with higher education levels are significantly at lower risk of depression compared to those with low education levels.

Other studies have reported a significant effect of marital status on depression in the elderly population [242-246]. It has been shown that widowhood or divorced marital status compared to married significantly increased the risk of depression especially in the older population. Our study also observed a similar relationship between marital status and depression in men with BPH. We observed that elderly widowed or divorced with BPH were at higher risk of depression compared to elderly married men with BPH. Further, among White men with BPH, the risk of depression was significantly higher in the widowed compared to the married elderly men. These findings suggest that loneliness and social isolation may influence depression in elderly men with BPH. A study by Alpass and Neville, 2003, demonstrated that a significant relationship exist between loneliness and psychological wellbeing of older males. They found that loneliness was the most significant factor associated with higher Geriatric Depression Scale score (GDS)

in their study population [247]. Another study also showed a 10-20% risk of developing depressive symptoms with the first years of bereavement [23].

One of the main strength of our study was that our study population was drawn from a national representative sample of elderly men with BPH in the United States. Secondly, we defined depression and BPH using both clinical (ICD-9 codes from claims data) and self-report (MCBS survey) information. However, our study has several limitations. This was a cross sectional study and therefore we could not ascertain causality in this association. A longitudinal study would be more suitable to determine the cumulative effect of "life-time view" of the social and economic factors on depression in elderly men starting from middle life. This will extend our understanding of whether cumulative disadvantage, with focus on socioeconomic heterogeneity, may explain the relationship between depression and BPH in elderly men. Secondly, our study sample was underpowered to detect effects of others on depression due to small sample size and majority were Whites with BPH. Thirdly, we did not have enough sample size to compare the differences in risk of depression between White elderly males with BPH and other races including Hispanics with BPH.

Conclusion

The findings from this study provide additional data to support the influence of socioeconomic context on the risk of depression in elderly men with BPH. Our data suggests that socioeconomic disadvantages may exist in association of BPH and depression in the elderly. Further epidemiologic research in a larger cohort is needed for a better understand the effect of socioeconomic heterogeneity on depression in elderly men with BPH. Social and economic cumulative advantage/disadvantage from early

lifetime may be plausible explanation of the difference in the health trajectory of the elderly population.

CHAPTER 5

CONCLUSION

Dissertation summary

Depression in the elderly is common among those with chronic diseases including cancer, diabetes, heart diseases and chronic obstructive airway diseases [1, 4, 23, 51, 69, 223]. Recently, several new reports suggested an effect of benign prostatic hyperplasia (BPH) on depression among aging men [108, 125-129]. BPH, a common problem with aging men, often presents with distressing lower urinary tract symptoms (such as frequent urination at night, difficulty in passing urine), which negatively affects the quality of life of elderly men [93-96, 98, 108, 125-129]. Studies that explored the association between BPH and depression in men are limited [108, 125-127]. However, these studies suggest that the risk of depression is higher among men with BPH or lower urinary tract symptoms, compared to those with no BPH [108, 125-127].

There are several research questions unanswered in the relationship between depression and elderly men and paucity of data remains an issue. We have tried to fill some gaps:

1. What is the prevalence of depression and BPH in elderly male Medicare beneficiaries, aged 65 years or above, and what factors are associated with depression reported among elderly male Medicare beneficiaries, 65 years or above, in the United States?

2. What is the rate of transition of elderly Medicare beneficiaries with no depression state to depression state and how does BPH influence the transition states of depression?

3. Does socioeconomic disadvantage influence the occurrence of depression in aging with BPH?

We hypothesized that the risk of depression was higher among elderly with BPH compared to those without BPH. Our second hypothesis was that BPH influences the transition states of depression. We also hypothesized that there was a significant effect of socioeconomic disadvantage on depression in elderly men with benign prostatic hyperplasia.

We conducted our study using the Medicare Current Beneficiary Survey (MCBS) data and physicians' claims data from 2005 through 2009. The MCBS is a nationally representative data conducted by the Center for Medicare and Medicaid Services (CMS). From the MCBS survey data, we defined depression from survey questionnaires as follows: (1) Any respondent who reported sad or depressed "all of the time" or "most of the time" and (2) sad or depressed "some of the time" and loss of interest. The third definition of depression was based on the International Classification of Disease, ninth edition Clinical Modification (ICD-9-CM) codes reported in the claims data. [38] BPH was determined using the response to MCBS survey on whether "Past year respondent was told he had enlarged prostate/BPH" ("yes" or "no"). Second instrument was the clinically diagnosed BPH using the ICD-9-CM codes reported in the claims data. The MCBS survey data also contained information on socio-demographic characteristics and comorbidities including cancer other than skin cancer, arthritis, diabetes, heart diseases and mental health diseases other than depression. To address our second research question, we constructed transition time points using the year variable in the MCBS data. In addition, we defined Markov state for depression (no depression in both years, no

depression to depression, depression to no depression, and persistent depression states), and BPH (no BPH for both years, no BPH to BPH, BPH to no BPH, and persistent BPH states).Our third research question was addressed using the sample of only elderly men with BPH.

The results showed a significantly higher risk of depression in elderly men with BPH compared to those without BPH. Even among those without coexisting medical conditions like cancer, diabetes, heart diseases, and arthritis, the risk of depression increased by 70% in those with BPH compared to elderly with no BPH. Further, having additional two or more comorbidities such as cancer, diabetes mellitus, and heart diseases increased the risk of depression by two folds in elderly with BPH compared with no BPH.

The second study revealed for the first time that the Markov process of depression is significantly influenced by the health status of BPH in elderly men. We observed the following in the transition analysis : 1) progressing from BPH to no-BPH Markov process significantly increased the transition rate from depressed to non-depressed states in elderly men, 2) having persistent BPH compared remaining with no-BPH is associated with about 40% increased risk of moving to persistent depression than remaining is no-depression state. 3), moving from no-BPH to BPH health state increased the transition rate from no-depression to depression state but not statistically significant. Our third study demonstrated that elderly men with BPH and high-income or high-education levels were at significantly lower risk of depression than those in the lower income group or low education levels. Overall being married provided a protective effect for depression than widowed or divorced/separated in the elderly male population.

Strengths and limitations

The strengths of this dissertation research include: first, we used a cohort data from the survey conducted in a large national representative sample of elderly men in the United States. Second, definitions of the depression and BPH were done using both self-reported data and clinically confirmed diagnosis. The survey data was drawn from the MCBS data conducted yearly among elderly Medicare beneficiaries from ages 65 years or above, and among those with disability. The clinical information was obtained from the Medicare claims database built for billing purpose. The third strength of our study was using the Markov modelling approach to examine the relation between BPH status and depression progression in our study population. The time order established in the transition analysis may help establish a cause-effect relationship between BPH and depression in this study population. Unlike survival analysis, the Markov's modeling is a natural modeling technique with minimal assumptions. Lastly, we adjusted for characteristics like medical conditions (cancer, heart diseases, diabetes, arthritis and cancer), and socio-demographic variables that may confound the association between depression and BPH in elderly population.

The drawbacks of our study are: (1), our dataset was drawn from a short follow up data therefore detecting developments or changes in the characteristics of the target population at both the group and the individual level is difficult. (2) All our study subjects had either Medicare insurance or other private insurance, so findings may not be generalizable to the uninsured population of elderly men. (3) The racial distribution of the study population is skewed with Whites being disproportionately more than other races. This may have resulted in some of the findings observed in White elderly men with BPH.

Except for Blacks with BPH, we were unable to compare effects of socioeconomic heterogeneity between Whites men with BPH and other racial groups including Hispanics. (4) Information about LUTS symptoms and depression was not provided. Therefore, we could not assess the effect of severity of BPH on depression. (5) Several factors would have influenced the Markov process in our study. For instance, we did not control for factors such as whether the respondent was receiving treatment during the follow-up period, the type of treatment and treatment adherence that may have influenced progression of depression or BPH. (6) An important limitation of Markov model is the "memoryless" feature of Markov process, i.e. the probability of moving out is independent of the state the patients may have experienced before entering that state. Lastly, the sensitivity of depression screening used in the MCBS questionnaire is unknown.

Clinical implications and recommendations

Our findings have strong implications for clinical management of elderly men with depression. Evidence supports that depression is often undetected or undertreated in the clinics. In addition to chronic medical comorbidities in elderly men, the presence of BPH may significantly increase the risk of depression in this population. Therefore, elderly men with BPH should be carefully evaluated for depressive symptoms especially in the primary care settings to reduce further disability from persistence of BPH and depression. Findings from our transition analysis suggest that progressing from BPH health state to state without BPH is significantly associated with transition from depressed to non-depressed state. One of the possible explanations may be due to treatments received during the study period. However, our study suggests that prompt

corrective intervention for BPH symptoms may be needed to moderate the progression of depression in elderly men.

Public health implication and recommendations

In recent years, reports have suggested a growing population of aging people both in the US and elsewhere. This implies a possible rise in the prevalence of chronic diseases such as depression, diabetes mellitus, heart diseases, cancer, arthritis and mental health conditions. This dissertation addressed an important concern among aging men, the relationship between BPH and depression in late life. More research is necessary to understand the biological pathways and genetic explanation for the association of BPH and risk of depression in elderly men. Several reports suggest that depression is associated with disability and low health quality of life in the older population. Therefore, we recommend that adequate research in this area is critical to mitigate the impact of BPH and depression on the quality of life of the aging men.

Suggestions for future research

This is the first attempt that explored the transition probability of Markov processes of depression and BPH in the population of US elderly men. We found that BPH states as well as socioeconomic indices significantly influence the progression of depression in elderly men. However, further research applying other epidemiological methods and socioeconomic indices is needed to validate our findings in a different population. In addition, epidemiologic research with a focus on cumulative advantage/disadvantage from early lifetime should be considered to get a better understanding of health trajectory in the elderly population. Lastly, future research could

explore how the severity of lower urinary tract symptoms of BPH could affect the transition in depression severity.

GLOSSARY

Depression: is a mood disorder that causes a persistent feeling of sadness and loss of interest.

Late life depression (LLD): First diagnosis of depression after 65 years old

Benign prostatic hyperplasia (BPH): Noncancerous-enlargement of the prostate gland. Also referred to as benign prostatic enlargement

Lower urinary tract symptoms (LUTS): refers to symptoms due to abnormality or compression of the ureters, urinary bladder and urethra resulting in poor stream, hesitancy, terminal dribbling and incomplete voiding.

Chronic diseases: Medical conditions lasting for more than three months

Beneficiary: Refers to anyone enrolled in Medicare, regardless of use of services

Chronic obstructive airway disease: Refer to a group of lung diseases that block airflow and make breathing difficult. Examples are emphysema and chronic bronchitis

Diabetes mellitus: A group of diseases that affect how the human body uses glucose, commonly called blood sugar. This condition includes Type 1 and II diabetes

Heart disease: is one of several cardiovascular diseases (diseases of the heart and blood vessel system) affecting the heart. Other cardiovascular diseases include stroke, high blood pressure, angina (chest pain), and rheumatic heart disease.

Osteoarthritis: degeneration of joint cartilage and the underlying bone. It is commonly associated with aging. It causes pain and stiffness, especially in the hip, knee, and thumb joints. Also referred to as arthritis

Cancer: Diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to penetrate and destroy normal body tissue.

Comorbidity: The presence of one or more additional disorders (or diseases) co-occurring with a primary disease or disorder

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