PREVALENCE AND FACTORS ASSOCIATED WITH THE PRESENCE OF DEPRESSION AMONG OLDER ADULTS WHO REPORT PAIN: FINDINGS FROM THE MEDICARE HEALTH OUTCOMES SURVEY

By

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ABSTRACT

Objective: This study investigates whether older adults have increased odds of self-reported depression in the presence of self-reported pain and whether these odds of depression differ for males and females.

Methods: A historical cohort survey using 75,015 Medicare managed care enrollees who responded to the Health Outcomes Survey. Enrollees who reported pain at baseline and at follow-up two years later were compared to enrollees who reported no pain at both time points. All enrollees were assessed for positive depression screens at follow-up.

Results: There are increased odds of self-reported depression for both males and females who self-report pain, even after controlling for age, race, education, smoking, cancer treatment, and SF-36 mental and physical health domains. Males are 93 percent more likely to report depression in the presence of pain than in the absence (OR 1.93, 95% CI: 2.0-2.0), while females are 59 percent more likely to report depression in the presence of pain than in the absence (OR 1.59, 95% CI: 1.6-1.6.

Conclusions: Older adults who self-report pain should be considered for risk of depression. This study provides evidence that, among older adults, females have higher odds of depression compared to males; both in the presence of pain and without. However, in the presence of pain, males experienced a larger increase in their odds of depression than females, a near doubling. These findings suggest that questions by healthcare providers regarding pain could lead to more targeted and effective depression screenings for at-risk older adults.

Research Question

Among Medicare Advantage enrollees, does self-reported pain increase odds of self-reported depression?

Primary Hypothesis

Odds of depression at follow-up will be higher among older adults who report pain at both baseline and follow-up, after adjustment for demographics, comorbid conditions, ADL restrictions, and baseline depression.

Secondary Hypothesis

Pain will interact with gender in predicting odds of depression at follow-up, after adjustment for baseline depression, demographics, comorbid conditions, and ADL restrictions.

Specific Aims

Using cohort years 2004 and 2005 totaling approximately 110,000 Medicare Advantage (MA) enrollees with follow-up, this study will;

1) Identify surveyed MA enrollees who reported pain at both baseline and follow-up or no pain at both points in both cohorts.
2) Identify baseline demographic characteristics for surveyed MA enrollees with substantial follow-up, such as age group, gender, race, marital status, education level, and body mass index.

3) Develop a multivariable logistic regression model to estimate the odds of depression for MA enrollees, while controlling for demographic characteristics.
4) Test the hypothesis that the odds of depression are higher among MA enrollees with pain, after adjustment for baseline depression and other characteristics.

Background

Figures on the prevalence of pain affecting older adults range from 30 to 68 percent.[1, 2] While evidence suggests that older adults have lower prevalence of pain compared to those younger than them, there is also evidence that the chronicity of pain is longer among older adults compared to rest of the population.[3] Among older adults, prevalence continues to demonstrate an increase with age.[1] Furthermore, in 80 percent of cases when pain is experienced, it continues to be experienced six months later.[4] With pain being experienced by many older adults, and with an increasingly larger older population in the US and the rest of the world and increasing numbers of older adults confront chronic and degenerative conditions such as arthritis, osteoporosis, cancer, and diabetes, there is a growing need to understand the epidemiology of pain.

Many researchers have studied the relationship between pain and depression among older adults. The interaction of these two conditions and the order in which they precede each other has led to many "chicken versus egg" comparisons.[5] What is known regarding depression among older adults is that: 1) subsyndromal depressive symptoms are far more common than full-fledged major depression as

diagnosed with DSM-IV criteria; and 2) the prevalence of major depression among older adults declines with age, while depressive symptoms increase.[6] An estimated 5 million older adults have subsyndromal depression symptoms. [7] These subsyndromal depressive symptoms have been identified in 8 to 20 percent of older community residents.[5] Unsurprisingly, subsyndromal depressive symptoms are associated with an increased risk of developing major depression.[6] However, these symptoms and syndromes continue to be under-recognized and under-treated and, as a result, older adults have an excess risk of morbidity and mortality as well as an increased risk of suicide.[6] Additionally, the risk of depression in the elderly increases with other illnesses and when ability to function becomes limited.[7] Thus, while depression may be less prevalent among older adults, it continues to have serious negative effects, including increased burden of physical illness, impaired functioning, and risk suicide.[8]

Depression has also been associated with many other demographic, health behavior, and medical factors. In order to accurately evaluate the effect of pain upon depression many of these other factors need to be concurrently assessed if possible. An individual's race may be associated with depression with, African-American's having higher rates for major depressive disorder than non-Hispanic whites.[9] Higher levels of education are shown to reduce risk of depression; older adults with less education have a relative risk of depression 1.5 times as great compared to older adults with more education.[10] Marital status is associated with depression; older adults who were never married or were previously married have a 30 percent

greater risk of depression morbidity compared to older adults that are currently married.[11] Obesity (BMI ≥ 30) is associated with depression such that adults with current depression (Odds Ratio = 1.7) or a lifetime diagnosis of depression (OR = 1.6) are significantly more likely to be obese than those without those diagnoses.[12] Similar findings have also been found for smoking where adults with current depression (OR = 2.7) or a lifetime diagnosis of depression (OR = 1.7) are significantly more likely to be current smokers than those without depression.[12] Lastly, cancer treatment is associated with depression; adults receiving cancer treatment in the past month are 53 percent more likely to report psychological distress (which includes depression and anxiety) compared to those without cancer.[13]

The relationship between pain and depression among older adults is complicated by the host of other factors that interact with both pain and depression. Pain is associated with many chronic and degenerative conditions and assessing pain is further complicated by the occurrence of comorbidities. The assessment of depression is complicated by the same factors. There is evidence that older adults with mobility disability and limitations in instrumental activities of daily living have increased risk of depression.[14, 15] Indeed, there is evidence that depressive symptoms below the threshold of subsyndromal depression are associated with increased disability burden among older adults.[16] The cumulative impact of comorbidities has been shown to result in increased reports of pain and depressive symptoms in addition to reduced activity levels and higher physical impact from

pain.[17] Indeed, a strong, linear association has been found regarding the number of chronic conditions and depressive symptoms.[18] This same research found evidence that osteoarthritis, rheumatoid arthritis, and stroke were strongly associated with psychological distress (including depressive symptoms), supporting the notion that chronic conditions resulting in more functional limitations have stronger impact than chronic conditions resulting in less functional impairment (such as diabetes or some cancers). More recent evidence has shown that some of these chronic conditions can be explained by poor self-reported health and functional status, highlighting the complexity of this research. [19] This research demonstrates that in order to effectively evaluate pain as a risk factor for depression, impairments in activities of daily living and chronic conditions need to be evaluated concurrently.

Lastly, depression can have differing effects between the genders. Evidence shows that females have higher prevalence rates of depression in later life than males (25 percent vs. 18 percent).[11] Also, older females are generally more likely to report depressive symptoms than older males.[20] The modification of depression by gender should be incorporated into studies that seek to assess depression in order to prevent confounding. The improved understanding gained from learning to what degree gender modifies the effect of pain upon depression can lead to more efficacious treatments for older females and males.

Methods

Data Source

This historical cohort study uses Medicare Health Outcomes Study (HOS) response data for cohort years 2004-2006 and 2005-2007. These two cohort years represent Cohort 7 and Cohort 8, respectively, for the Medicare HOS. The Medicare HOS has been conducted in the spring of each year since 1998. Each year, the Medicare HOS conducts baseline assessments of Medicare Advantage enrollees; these respondents form the initial cohorts. Two years later, the baseline respondents are reassessed. Approximately 160,000 randomly sampled MA enrollees are surveyed at baseline years in each cohort. At follow-up, two years later, each cohort has approximately 60,000 enrollees with completed surveys. Surveys are considered completed if enrollees respond to at least one question.

The Medicare HOS was developed to measure the quality of life and functional health status of Medicare beneficiaries enrolled in managed care. The HOS also enables Medicare to monitor and evaluate the quality of care and services provided to Medicare managed care enrollees and provide information that permits plan-to-plan comparison.

As Table 1 demonstrates, the Medicare HOS cohort population is similar to the general Medicare population in regards to age, gender, race, marital status, and education demographics. The study sample for HOS data includes more older adults than the general Medicare population. This is likely because the managed care

population that comprises Medicare Advantage has proportionally fewer individuals with disabilities, who are on average younger than most MA enrollees.

Table 1: General Medicare population compared with Medicare HOS cohorts and final sample

	General Medicare population, % *	Medicare HOS cohorts 2004-05, %	Final sample, %
Number	-	83,555	75,015
Age			
Less than 65	14.4	6.5	6.2
65-74	44.3	50.0	50.9
75 and older	41.3	43.5	42.9
Race			
Caucasian	86.3	88.0	88.8
African-American	9.6	7.0	6.6
Other	4.1	4.9	4.6
Gender			
Male	44.0	40.5	41.0
Female	56.0	59.5	59.0
Marital Status			
Married	51.8	56.4	57.0
Non-married	48.2	43.6	43.0
Education Level			
Less than HS education or GED	30.4	25.8	24.5
HS education or GED	30.4	38.6	38.9
Greater than HS education or GED	39.2	35.7	36.5

* Medicare demographics data from Centers for Medicare and Medicaid Services, *Health & Health Care of the Medicare Population: 2003*. Includes disabled and non-elderly.

The Medicare HOS is composed of five components;

- A health survey instrument
- Demographics

- Chronic medical conditions
- Activities of daily living (ADLs)
- Depression screen

Until 2006, the Medical Outcomes Survey (MOS) 36-Item Short Form Health Survey (SF-36) instrument was used at both baseline and follow-up. Beginning in 2006, new cohorts were assessed at baseline using the Veterans RAND 12-Item Health Survey (VR-12) instrument. Also beginning in 2006, follow-ups to previous cohort were assessed using the VR-12 in order to reduce the burden upon surveyed MA enrollees. Thus, both cohorts in this study were assessed at baseline with the SF-36 and at follow-up with the VF-12 instrument. The SF-36 and VR-12 measure the same health domains. In both the SF-36 and VR-12 instruments, questions may be aggregated into one of eight scales which in turn may be used to calculate overall physical and mental health summary measures;

- Physical functioning (PF)
- Role-physical (RP)
- Role-emotional (RE)
- Bodily pain (BP)
- Social functioning (SF)
- Mental health (MH)
- Vitality (VT)
- General health (GH)

The SF-36 has been shown to consistently and reliably measure heath status and functioning in many US populations as well as in other countries.[21, 22, 23, 24] The SF-36 has also been validated among the HOS population (using Cohort 1) and shown to provide internally consistent results within the eight scales. [25] Additionally, the SF-12 has been validated as an equivalent measure to the SF-36 and the summary measures may be reliably compared.[26] Lastly, there is evidence that the SF-36 has a high positive predictive value in classifying depression using the mental health summary measure in chronic pain patients.[27]

Medicare HOS Management

The Medicare HOS is implemented by the National Committee for Quality Assurance (NCQA) under contract with the Centers for Medicare and Medicaid Services (CMS). Each year Medicare managed care plans contract with NCQA-certified vendors to carry out the Medicare HOS once the sample has been selected and approved by CMS. [28] Survey vendors receive HOS survey administration training annually from NCQA in order to remain certified. Vendors then administer the HOS surveys according to NCQA protocol. Once the survey data have been collected, they are submitted to NCQA for consistency review.[28] The data are then submitted to Health Services Advisory Group (HSAG) for cleaning, aggregation, and analysis.[28]

Medicare HOS Cohort Enrollment

At baseline, MA enrollees were eligible for sampling by survey vendors using four criteria;

- For MA plans with more than 1,000 members, a simple random sample of 1,000 enrollees was used for the baseline survey.
- For MA plans with 3,000 or more members, enrollees who responded to a previous year's HOS survey were excluded from the current year's baseline sample.
- For MA plans with 1,000 members or less, all enrollees were selected for the baseline sample.
- Members from all plans were considered eligible if they had been continuously enrolled in the same plan at least six months and did not have End Stage Renal Disease.

MA enrollees were eligible for follow-up if they reported sufficient data to derive PCS or MCS scores at baseline. Survey vendors excluded enrollees from follow-up if the enrollee had disenrolled from their MA plan or had deceased following the baseline survey.

The 2004-2006 cohort survey vendors identified 157,558 enrollees in the baseline survey, with 106,306 enrollees completing the baseline survey (67.5% response rate). At time of follow-up, 74,989 of the baseline respondents remained eligible for follow-up, with 61,137 enrollees completing the follow-up survey (81.5% response rate).

The 2005-2007 cohort survey vendors identified 160,902 enrollees in the baseline survey, with 108,692 enrollees completing the baseline survey (67.6% response rate). At time of follow-up, 71,975 of the baseline respondents remained eligible for follow-up, with 57,324 enrollees completing the follow-up survey (79.6% response rate).

Study Enrollment

For this study, an additional requirement was applied regarding completeness of data; only enrollees who completed 80% or more of the follow-up survey questions were selected for analysis. This is referred to as "substantial follow-up." For the 2004-2006 cohort, 58,939 of the 61,137 MA respondents were retained (96.4% inclusion rate). For the 2005-2007 cohort, 54,732 of the 57,324 MA respondents were retained (95.5% inclusion rate). From respondents with substantial follow-up, cases selected for analysis included those who reported pain at both baseline and follow-up and those who reported pain at neither time, resulting in a total sample size of 83,555. A description of how pain is assessed in this analysis is provided under Measurement of Predictor Variables below.

Informed Consent and IRB Approval

The responses to the Medicare HOS are accessed from Medicare's public use files. Surveyed MA enrollees are de-identified and given unique nine-character randomly assigned alphanumeric identifiers. Furthermore, individual demographic data (age,

race, etc.) is categorized to ensure confidentiality. Since this study uses de-identified, public use data, it was eligible for and received an OHSU IRB waiver.

Measurement of Predictor Variables

Self-reported Pain

On the MOS SF-36 component, question 8 is a part of the bodily pain (BP) scale. The same question is asked at follow-up as part of the VF-12 where it is question 5.

> "*During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?*"

The question is measured using a 5-point Likert scale;

Not at all	A little bit	Moderately	Quite a bit	Extremely

MA enrollees with substantial follow-up who responded with "moderate" or greater pain at both baseline and follow-up, were categorized as having self-reported pain. MA enrollees who respond with "Not at all" or "A little bit" at both baseline and follow-up were categorized as <u>not</u> having self-reported pain. The numbers of respondents in each category of the resulting dichotomous pain predictor are shown in Table 2.

Table 2: Pain categories and MA enrollee response counts, by cohort

Cohort	Pain category	N
2004-2006	No pain @ Baseline and no pain @ Follow-up	27,384
	Pain @ Baseline and pain @ Follow-up	16,112
	Subtotal (73.8% inclusion rate)	43,496
2005-2007	No pain @ Baseline and no pain @ Follow-up	24,689
	Pain @ Baseline and pain @ Follow-up	15,370
	Subtotal (73.2% inclusion rate)	40,059
	Total	**83,555**

Covariates

There are several demographic measures (in Table 3) that were considered for model inclusion; most were determined by baseline responses.

Table 3: Demographic covariates and descriptions

Covariate	Description
Cohort	Cohort 7 (2004-2006) or Cohort 8 (2005-2007)
Age group	Less than 65, 65 to 74, and 75 and older
Race	White, Black or African-American, or Other
Gender	Male or Female
Marital Status	Married or Non-married
Education Level	Less than HS education or GED, HS education or GED, or greater than HS education or GED
Body Mass Index	Not obese (BMI < 30) or Obese (BMI ≥ 30) *

* This measure is assessed by the HOS only at follow-up.

The HOS contains additional questions at baseline and follow-up regarding the health of MA enrollees. Several HOS item responses regarding baseline arthritic pain, baseline self-rated health, and current or past history of cancer were converted into dichotomous or categorical variables. These variables were also evaluated for model inclusion.

Additionally, there were HOS questions regarding the presence of restrictions performing ADLs and the presence of co-morbid conditions at baseline. The responses to these multiple questions were formed into categorical variables that were generated to indicate presence and severity of co-morbid conditions and the number of restrictions on ADLs, ranging from 0 through 6.

The responses to the six HOS questions regarding restrictions performing ADLs were converted into a categorical variable that represented the sum of ADLs questions with positive responses. There were 13 HOS questions regarding co-morbid conditions where the physician had informed the MA enrollee of the diagnosis. Those responses were also converted into a categorical variable that indicated the presence of a co-morbid condition(s) and the highest degree of association with mortality among present conditions. Categories of association with mortality included: 1) not associated, 2) possibly associated, and 3) associated. Table 4 shows the co-morbid conditions and the level of association to mortality they are assigned. The categories and assignments are based on work by Kaplan et al.[29] The categorical co-morbid conditions variable was also considered for model inclusion.

Table 4: Co-morbid conditions in HOS and their association with mortality

No reported chronic conditions	One or more conditions not assoc. w/ mortality	One or more conditions possibly assoc. w/ mortality	One or more conditions assoc. w/ mortality
No response to any chronic condition questions	Arthritis of the hip/knee	Emphysema, asthma, or COPD	Hypertension or high blood pressure
	Arthritis of the hand/wrist	Crohn's disease, ulcerative colitis, or inflammatory bowel disease	Angina pectoris or coronary artery disease
	Sciatica		Congestive heart failure
			A myocardial infarction or heart attack
			Other heart conditions (heart valve problems or irregular rhythm)
			Cancer (other than skin cancer)
			A stroke
			Diabetes

Additionally, the eight SF-36 scales created from the MOS SF-36 item responses at baseline were considered for model inclusion. Many of the MOS SF-36 questions in the HOS are posed in a positive manner and scaled to indicate better health and higher health-related quality of life (HRQOL) with increasing score. However, some questions are posed in the reverse and scaled to indicate poorer health and lower HRQOL, the item responses to these questions were recast in order to create and score the SF-36 physical and mental health scale. The result is that all eight SF-36 scales, each ranged from 0-100, are standardized and all the health domains uniformly indicate improved health and better HRQOL with higher scores.

Measurement of Outcome Variable

Self-reported Depression

The Medicare HOS contains a depression screen component. This component consists of three questions;

1. *In the past year, have you had 2 weeks or more during which you felt sad, blue or depressed; or when you lost interest or pleasure in things that you usually cared about or enjoyed?*
2. *In the past year, have you felt depressed or sad much of the time?*
3. *Have you ever had 2 years or more in your life when you felt depressed or sad most days, even if you felt okay sometimes?*

If an MA enrollee responds "yes" to *any* of the three questions, they are considered to have a positive depression screen. The depression screen was assessed at both baseline and follow-up. The follow-up depression screen was assessed as the outcome variable. The baseline depression screen was considered as a potential covariate.

Statistical Analysis

Statistical analyses were conducted with STATA v10.1.[30] Missing data for MOS SF-36 questions were analyzed in order to estimate SF-36 physical and mental scales. The half-scoring rule was used in scales containing missing item responses.[31] With the half-scoring rule, a scale is considered scorable if at least 50 percent of the items are completed. The missing items are prorated with the average score of the non-

missing items. The half-scoring logic was adopted from previous studies that performed similar analyses using the SF-36 physical and mental scales.

Review of HOS item responses to arthritic pain showed that one-third (33.3 percent) of enrollees in both cohorts failed to provide a response to this question and the covariate was dropped from the analysis. All other demographic and health status questions had much higher item response rates. Only MA enrollees with complete item responses to demographic and health status variables and valid generated variables (including generated SF-36 physical and mental health scales) were included for analysis. The final sample selected for analysis contained 75,015 MA enrollees with complete item data for all potential covariates. A multivariable logistic regression model was used to estimate the odds of depression for MA enrollees while controlling for demographic variables as well as controlling for other health status variables. In addition, tests were conducted for possible interactions among covariates for inclusion into the model if they met statistical significance. Lastly, the final model was assessed for fit using the Hosmer-Lemeshow test for goodness-of-fit and discrimination ability was evaluated with a ROC curve.[32]

Results

Study Population

The final sample contained 75,015 MA enrollees with complete item data for all potential covariates. Among these MA enrollees, 51 percent were between the ages of 65 and 74, while 43 percent were 75 or older. Also, 89 percent were Caucasian, 42 percent were male, and 57 percent were married. Educationally they were quite varied; a quarter had less than a high school education or GED, 39 percent had a high school education or GED, and the remaining 36 percent had education beyond those. As shown previously in Table 1, the MA enrollees included in the final sample for analysis were very similar to their general Medicare and cohort peers.

Estimated Unadjusted and Adjusted Model Results

All of the covariates initially considered for model inclusion demonstrated significant associations with depression at follow-up. As Table 6 demonstrates, significant crude (unadjusted) associations existed between odds of depression and categorical covariates, such as race and education level.

Since all initial covariates demonstrated significant crude association with depression at follow-up, all covariates were included in a full multivariable model to be assessed for association with depression at follow-up (also see Table 6).

The full multivariable model includes an additional covariate that tests for an interaction between pain and gender with respect to depression.

Table 6: Crude and adjusted model results for odds of depression among MA enrollees with pain

n=75,015					
	Crude [1]		Adjusted [2]		
	OR	95% C.I.	OR	95% CI	*p* -value
Pain (Yes)	5.82	(5.63-6.03)	1.97	(1.79-2.17)	<0.001
Demographic Covariates					
Gender (Female)	1.38	(1.34-1.43)	1.38	(1.29-1.46)	<0.001
Pain (Yes) x Gender (Female)			0.83	(0.76-0.90)	<0.001
Age group					
< 65	Referent	-	Referent	-	-
65-<75	0.14	(0.13-0.15)	0.61	(0.56-0.66)	<0.001
75+	0.17	(0.16-0.18)	0.58	(0.53-0.64)	<0.001
Race					
White	Referent	-	Referent	-	-
African-American	1.65	(1.55-1.75)	1.14	(1.05-1.24)	0.001
Other	1.25	(1.16-1.35)	1.09	(0.99-1.20)	0.084
Marital status (Not married)	1.50	(1.45-1.55)	1.02	(0.98-1.07)	0.359
Education level					
Less than High School	Referent	-	Referent	-	-
High School / G.E.D.	0.64	(0.61-0.66)	0.88	(0.84-0.93)	<0.001
More than High School / G.E.D.	0.52	(0.50-0.54)	0.91	(0.86-0.96)	0.001
BMI category (BMI ≥ 30)	1.63	(1.57-1.69)	1.04	(0.99-1.09)	0.111
Other Health-Status Covariates					
Baseline depression (Yes)	12.35	(11.89-12.84)	4.19	(4.00-4.39)	<0.001
Baseline smoking (Yes)	1.79	(1.71-1.88)	1.27	(1.19-1.35)	<0.001
Cancer treatment at baseline (Yes)	1.20	(1.12-1.29)	1.03	(0.94-1.12)	0.544
Cancer treatment since baseline (Yes)	1.24	(1.14-1.35)	1.28	(1.15-1.43)	<0.001
Baseline ADL count (1.5) *	1.56	(1.55-1.58)	1.01	(0.98-1.04)	0.515
Baseline highest chronic comorbidity group					
No reported chronic conditions	Referent	-	Referent	-	-
One or more conditions not assoc. w/ mortality	1.94	(1.79-2.11)	1.05	(0.95-1.16)	0.316
One or more conditions possibly assoc. w/ mortality	3.15	(2.82-3.50)	1.22	(1.07-1.40)	0.003
One or more conditions assoc. w/ mortality	2.51	(2.36-2.68)	1.07	(0.99-1.15)	0.095

Table 6: Crude and adjusted model results for odds of depression among MA enrollees with pain (cont.)

n=75,015					
	Crude [1]		Adjusted [2]		
	OR	95% C.I.	OR	95% CI	*p*-value
Baseline SF-36 Physical and Mental Health Scales					
Physical functioning (30.0) **	0.46	(0.46-0.47)	1.00	(0.97-1.04)	0.947
Role-physical (43.7) **	0.44	(0.43-0.45)	1.01	(0.98-1.05)	0.463
Role-emotional (38.0) **	0.42	(0.42-0.43)	0.89	(0.87-0.91)	<0.001
Bodily pain (27.8) **	0.40	(0.39-0.41)	1.02	(0.97-1.06)	0.464
Social functioning (26.4) **	0.37	(0.36-0.37)	0.90	(0.87-0.92)	<0.001
Mental Health (18.5) **	0.29	(0.28-0.29)	0.59	(0.57-0.61)	<0.001
Vitality (23.2) **	0.37	(0.36-0.38)	0.91	(0.87-0.94)	<0.001
General health (22.2) **	0.39	(0.38-0.40)	0.96	(0.92-0.99)	0.008

[1] All odds ratios have a *p*-value < 0.001.
[2] All odds ratios adjusted for all listed variables.
* Per standard deviation (in parentheses); scale 0 - 6.
** Per standard deviation (in parentheses); scale 0 - 100.

The final model was created using backward elimination. Several of the covariates that indicated significant crude association did not have similar results when included in the full multivariable model.

Several of the covariates were highly correlated with other covariates and dropped in favor of a more meaningful variable. The lack of significance for three of the SF-36 scales in the final model (physical functioning, role-physical, and bodily pain) was due to their collinearity with the primary predictor variable of self-reported pain. Post-hoc analyses confirmed this, finding strong correlations with self-reported pain (Pearson's correlation of -0.68, -0.71, and -0.87 respectively).

Additionally, the model-building process revealed a lack of significance for the generated covariate for restrictions performing ADLs. This was likely due to 61 percent of the analyzed MA enrollees having not provided a positive response to a single ADL question and only 15 percent having responded positively to 3 or more ADLs questions (of a total of 7). Also, the generated covariate for ADLs showed a moderate correlation to the primary predictor variable of self-reported pain (Pearson's correlation of 0.59).

Lastly, the model-building process revealed a lack of significance for the generated covariate for co-morbid conditions. This was likely due to the 76 percent of analyzed MA enrollees with a co-morbid condition that is considered to be associated with mortality. The restricted variability prevented this variable from showing significance amidst other covariates. The distortion in this covariate was likely due to the high prevalence of hypertension (61%) in the analyzed MA enrollees. The prevalence of hypertension in the full 2004-2006 and 2005-2007 MA cohorts was nearly identical (61.3%).

The remaining covariates explored for crude association with depression were included in the final model-building process. Consideration was also given for an interaction between pain and gender to test the secondary hypothesis of a significant interaction between these two covariates.

Final Model Results

As Table 8 illustrates, in the final multivariable model resulting from the model-building process, self-reported pain at baseline was a strong and significant predictor of odds of depression at follow-up with an odds ratio (OR) of 1.93 (95% Confidence Interval: 1.79-2.08). This OR indicates that, among older adults enrolled in MA, males that reported pain at both baseline and follow-up two years later were 1.9 times as likely to have a positive depression screen response at follow-up as males that did not report pain at both time points. Since there was a significant interaction involving gender and pain, the OR of 1.93 is limited to males; the OR of 1.59 for females must incorporate the interaction. How the odds of depression for females were estimated is shown in the interaction's results.

This finding supports the primary hypothesis that the odds of depression at follow-up were higher among older adults who reported pain at both baseline and follow-up, after adjustment for baseline depression and other characteristics. This effect is rather large considering that this model accounted for other potential risk factors, including demographics and other physical and mental health measures.

Table 8: Final model results for odds of depression among MA enrollees with pain

n=75,015			
	Adjusted OR	**95% CI**	***p*-value**
Pain (Yes)	1.93	(1.79-2.08)	<0.001
Demographic Covariates			
Gender (Female)	1.38	(1.30-1.47)	<0.001
Pain (Yes) x Gender (Female)	0.83	(0.76-0.90)	<0.001
Age group			
< 65	Referent	-	-
65-<75	0.61	(0.56-0.66)	<0.001
75+	0.58	(0.53-0.63)	<0.001
Race			
White	Referent	-	-
African-American	1.15	(1.06-1.24)	0.001
Other	1.08	(0.98-1.19)	0.101
Education level			
Less than High School	Referent	-	-
High School / G.E.D.	0.88	(0.84-0.93)	<0.001
More than High School / G.E.D.	0.91	(0.86-0.96)	0.001
Other Health-Status Covariates			
Baseline depression (Yes)	4.21	(4.02-4.41)	<0.001
Baseline smoking (Yes)	1.26	(1.19-1.35)	<0.001
Cancer treatment since baseline (Yes)	1.28	(1.15-1.42)	<0.001
Baseline SF-36 Physical and Mental Health Scales			
Role-emotional (38.0) *	0.89	(0.87-0.92)	<0.001
Social functioning (26.4) *	0.90	(0.87-0.92)	<0.001
Mental Health (18.5) *	0.59	(0.57-0.61)	<0.001
Vitality (23.2) *	0.91	(0.88-0.94)	<0.001
General health (22.2) *	0.95	(0.92-0.98)	0.003

* Per standard deviation (in parentheses); scale 0 - 100.

As mentioned, this study also found that the strength of the relationship between pain and depression is modified by gender. Shown in Table 8 was a significant interaction between pain and gender. As a further indication of the different expressions of depression by gender, Table 9 shows how this study's prevalence of reported depression at baseline is higher for females (28.1 percent) compared to males (21.6 percent).

Table 9: Prevalence of reported depression at baseline, by gender

Gender		Reported depression, at baseline					
		No		Yes		Total	
		n	%	n	%	n	%
	Males	24,117	78.4%	6,635	21.6%	30,752	41.0%
	Females	31,803	71.9%	12,460	28.1%	44,263	59.0%
	Total	55,920	74.5%	19,095	25.5%	75,015	100.0%

This difference in prevalence between the genders is consistent with gender differences found in other studies referenced in the background portion of this study. In Table 10 the differing odds in favor of depression as determined by pain status for males and females show the specifics of the interaction.

Table 10: Effect modification for odds of depression by pain and gender among MA enrollees

Odds in favor of reported depression at follow-up *				
	Males		**Females**	
No Pain	0.076	(0.07 - 0.08)	0.106	(0.10 - 0.11)
Pain	0.147	(0.14 - 0.16)	0.169	(0.16 - 0.18)

* Estimated for an older white adult aged 65-74, with no baseline depression, no baseline smoking, no new cancer treatment, a HS education or GED, and a median role-emotional (100), social functioning (100), mental health (84), vitality (60), and general health (65) scale score.

Using the figures in Table 10 it is possible to view depression from two angles: gender and pain status. By comparing females to males, the interaction shows that in the absence of reported pain females are 38 percent more likely to report depression than males (OR 1.38, 95% CI: 1.4-1.4). In the presence of reported pain, females are only 15 percent more likely to report depression. (OR 1.15, 95% CI: 1.1-1.1).

Viewing this interaction from the other angle compares reported pain to no reported pain. From this angle males are 93 percent more likely to report depression in the presence of pain than in the absence (OR 1.93, 95% CI: 2.0-2.0), while females are 59 percent more likely to report depression in the presence of pain than in the absence (OR 1.59, 95% CI: 1.6-1.6)

This finding supports the secondary hypothesis that pain will interact with gender in predicting odds of depression at follow-up, after adjustment for baseline depression and other characteristics.

Table 11: Final model results for odds of depression among MA enrollees with pain, stratified by gender

	Males (n=30,752)			Females (n=44,263)		
	Adjusted OR	95% CI	*p* -value	Adjusted OR	95% CI	*p* -value
Pain (Yes)	1.85	(1.69-2.03)	<0.001	1.64	(1.53-1.76)	<0.001
Demographic Covariates						
Age group						
< 65	Referent	-	-	Referent	-	-
65-<75	0.66	(0.58-0.75)	<0.001	0.57	(0.51-0.64)	<0.001
75+	0.65	(0.57-0.74)	<0.001	0.54	(0.48-0.61)	<0.001
Race						
White	Referent	-	-	Referent	-	-
African-American	1.22	(1.06-1.40)	0.007	1.11	(1.01-1.23)	0.028
Other	1.15	(0.99-1.33)	0.074	1.05	(0.93-1.19)	0.445
Marital status (Not married)	1.09	(1.01-1.18)	0.030	1.00	(0.95-1.06)	0.993
Education level						
Less than High School	Referent	-	-	Referent	-	-
High School / G.E.D.	0.89	(0.81-0.97)	0.006	0.88	(0.82-0.93)	<0.001
More than High School / G.E.D.	0.87	(0.80-0.95)	0.002	0.94	(0.88-1.01)	0.073
Other Health-Status Covariates						
Baseline depression (Yes)	4.01	(3.70-4.35)	<0.001	4.30	(4.05-4.55)	<0.001
Baseline smoking (Yes)	1.23	(1.11-1.36)	<0.001	1.28	(1.18-1.39)	<0.001
Cancer treatment since baseline (Yes)	1.23	(1.05-1.44)	0.009	1.31	(1.13-1.53)	<0.001
Baseline SF-36 Physical and Mental Health Scales						
Role-emotional (36.9/38.7) *	0.91	(0.87-0.94)	<0.001	0.89	(0.86-0.92)	<0.001
Social functioning (25.6/28.9) *	0.87	(0.83-0.91)	<0.001	0.91	(0.88-0.95)	<0.001
Mental Health (18.4/18.5) *	0.60	(0.57-0.63)	<0.001	0.59	(0.56-0.61)	<0.001
Vitality (23.1/23.2) *	0.89	(0.84-0.94)	<0.001	0.92	(0.88-0.96)	<0.001
General health (22.3/22.1) *	0.95	(0.90-1.01)	0.075	0.95	(0.92-0.99)	0.019

* Per standard deviation (in parentheses, Males/Females); scale 0 - 100.

Table 11 shows the odds of depression in the presence of pain stratified by gender. The ORs in this gender-stratified table are similar to the non-stratified ORs in the final presented earlier (Table 8). The gender-stratified odds of depression in the presence of pain for males are 85 percent higher than in the absence, compared to

93 percent in the non-stratified model. For females, the gender-stratified odds of depression in the presence of pain are 65 percent higher than in the absence, compared to 59 percent in the non-stratified model.

In the gender-stratified results shown in Table 11, marital status was re-introduced as a covariate. As previously mentioned in the background, marital status has been shown to be associated with depression. However, in this study, marital status only demonstrates a significant relationship among males (*p*-value = 0.03) and is not significant among females. The marital status OR means that unmarried males have a 9 percent higher odds of depression compared to married males.

Table 12: Marital status at baseline, by gender

Gender		Marital status, at baseline					
		Married		Not Married		Total	
		n	%	n	%	n	%
	Males	23,240	75.6%	7,512	24.4%	30,752	100.0%
	Females	19,512	44.1%	24,751	55.9%	44,263	100.0%
	Total	42,752	57.0%	32,263	43.0%	75,015	100.0%

As shown in Table 12, in this study there is an approximately 45/55 split of marital status amongst females, while marital status is more unbalanced at 75/25 amongst males. It is unknown to what degree these differing proportions affected the marital status covariate in this study.

There are many demographic, health status, and SF-36 health scale covariates which were included in the final model to increase its predictive ability that also yielded significant results. In Table 8 the categorical demographic covariates of age, race, and education each showed significant effects across all their categories (Wald test $p < 0.001$ for each covariate). Age, even among older adults, continues to play a protective role against depression with those older than 75 having odds of depression 42 percent lower than those younger than 65. The race covariate confirmed findings from other studies and showed that whites had lower odds odd of depression than both African-Americans and those of "Other" race. Education remained protective but did not show a linear trend; while older adults with a high school diploma or a G.E.D. had lower odds of depression than those with less education, older adults with more than a high school diploma or a G.E.D. received less protective benefit from education.

Unsurprisingly, the health-related covariate of baseline depression status demonstrated the strongest relationship with depression at follow-up, with an OR of 4.2 (95% CI: 4.0-4.4). The other health-related covariates of baseline smoking and cancer treatment since baseline (i.e. emergent cancer treatment since baseline) were also significant, both yielding an OR of 1.3 (95% CI: 1.2-1.4).

The five retained SF-36 physical and mental health scale covariates were all significant. Each summary measure used a scale ranging from 0 through 100 and effect was measured using a step change of one standard deviation (1 SD). The

mental health scale showed the strongest relationship to depression; an increase in the measure by 1 SD (18.5) reduced the odds of depression by over 40 percent (p <0.001). Both role-emotional (1 SD = 38.0) and social functioning (1 SD = 26.4) scales showed reduced odds of depression by 11 and 10 percent, respectively (p <0.001 for both). Lastly, the remaining two SF-36 scales, vitality and general health, also had significant results; however, both had smaller effects with an increase of 1 SD (23.2 and 22.2, respectively) and only reduced the odds of depression by 9 (p <0.001) and 5 percent (p = 0.003), respectively.

Model Criticism

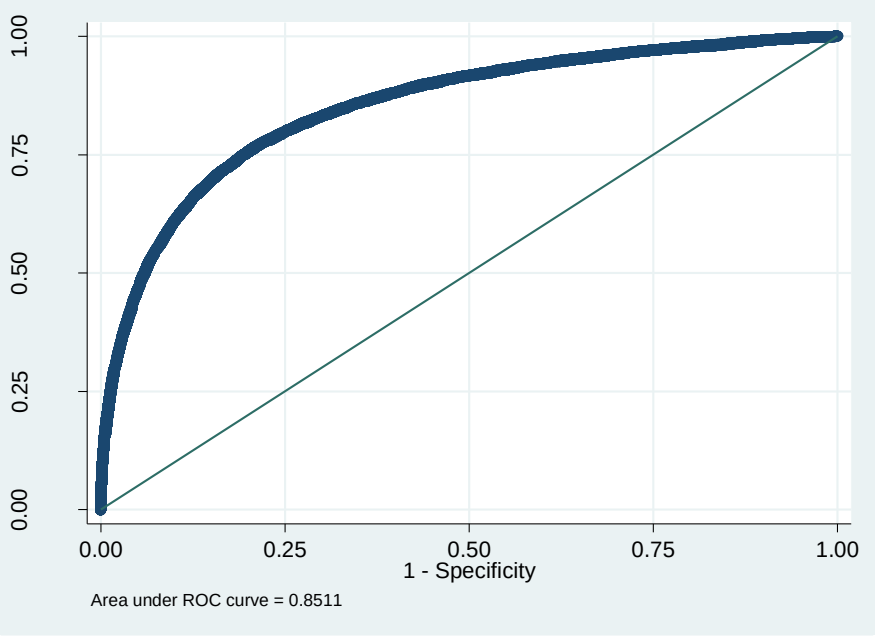
The Hosmer-Lemeshow (H-L) test was used to assess the goodness-of-fit between the observations contained in the final sample data and the expected values from the final model. The H-L test assesses whether or not observed values match expected values in subgroups of the model's population and yields a X^2 test statistic along with an accompanying degrees-of-freedom. However, due to the study's large sample size a single H-L test could not be used since it would erroneously indicate poor model fit because any discrepancies between observed and expected values would be magnified by the numerous observations, i.e. the H-L test was over-powered to detect minor flaws. To solve this problem, 10 sub-samples of randomly selected observations amounting to five percent (n=3,751) of the study's total sample population (n=75,015) were generated. On each of the sub-samples an H-L test for was conducted with subgroups of data in deciles. Eight of the 10 sub-samples yielded an H-L test with a p-value ≥ 0.10 which indicated that the final

model should not be rejected. Collectively, the H-L goodness-of-fit tests provided evidence of good model fit.

Additionally, a review of the 10 sub-samples showed that the estimated odds ratios for the various covariates demonstrated strong consistency across the sub-samples. While the odds ratios were not always statistically significant due to the much smaller sub-sample sizes, this consistency of estimated odds ratios was another indicator of the final model's predictive robustness.

Lastly, discrimination of the final model was evaluated and reported as a ROC area under the curve value of 0.85 (see Figure 1). A model with a ROC value ≥ 0.80 is considered to have "excellent" discriminative ability.

Figure 1: Final model ROC curve results



Discussion

This historical cohort study takes advantage of a large pre-existing dataset in order to tease apart factors contributing to depression, a condition that afflicts many older adults to varying degrees. The strong results from this study demonstrate highly significant odds of depression among older adults that experience pain.

Older adults with depression often report multiple complaints to their physicians, making it difficult to diagnose depression and provide treatment.[33] Furthermore, there is evidence that depression screening doesn't improve depression outcomes.[34] However, questions regarding pain directed to older adults may be more common due to the higher prevalence of chronic pain among older adults than compared to other populations.[3] These findings suggest that questions by physicians regarding pain could lead to more targeted and effective depression screenings for at-risk older adults.

This study's interaction provides further evidence that females have higher odds of depression compared to males; both in the presence of pain and without. However, in the presence of pain, males experienced a near doubling in their odds of depression (93 percent increase), while females only experienced an increase of 59 percent. This 17 percent reduction in the odds ratio for depression in females relative to males is statistically significant. The interaction's 95% CI indicates the marked difference that pain plays in increasing the odds of depression for males

(95% CI 0.76 - 0.90, or a relative reduction in odds of depression for females compared to males of between 24 percent and 10 percent).

This study's large sample size enabled the difference in odds of depression in the presence of pain between males and females to be brought into clear focus. While prior research has shown, and this study has confirmed, that older females have a prevalence and odds of depression higher than males, this study provides insight into the experience of males in the presence of pain and their sharp increase in odds of depression. Thus, while older females continue to experience higher odds of depression in presence or absence of pain, the effect of pain nearly doubling the odds of depression in older males represents a considerable public health concern.

It is also necessary to further research if current depression interventions among older adults yield differing benefit for males and females. The presence of an interaction raises the question of whether the efficaciousness of various interventions would differ between males and females among older adults.

The lack of significant findings for restrictions in performing ADLs and for physician-diagnosed co-morbid conditions illustrates the difficulty in accurately assessing so many individual variables at one time. These two measures had insufficient variability across the study population to accurately determine whether or not there was a relationship with depression. Future research should seek to

more clearly assess these variables in a broader population of older adults and determine their effect upon depression in the presence of pain.

There are some limitations to this study. The primary predictor variable was based on the HOS question regarding pain (SF-36 baseline and VR-12 follow-up bodily pain scale question), which referred to pain in the previous 4 weeks. Conversely, the depression screen referred to one year (first two screening questions) and two year (third screening question) timeframes. This incongruity of timeframes may have resulted in an overestimate of the effect of pain upon depression. By imposing the conditional requirement of pain at both baseline and follow-up (and comparing to enrollees without pain at both times) a similar timeframe comparison was created that reduced the impact of the difference in how the questions were posed. Nevertheless, an individual could experience pain of a different nature at follow-up than that experienced at baseline; this scenario would skew findings toward higher estimated odds of depression than truly exists.

Research shows females are 3.5 times as males as likely to bring up depression before their physician during an office visit.[35] If females are more likely to discuss depression in clinical settings than males, this could result in a bias against males in when screening is conducted by their physicians. It is unclear to what degree this study's significant interaction of pain and gender for depression would be affected if this possible female self-reporting bias were accounted for. Further research is needed to determine if this higher likelihood for females to discuss depression in a

clinical setting than males translates into a higher likelihood to self-report depression in a survey.

This study was also unable to measure the effect of drinking upon depression in this population since the HOS survey contains no questions regarding drinking status. There is evidence that individuals with current depression or a lifetime diagnosis of depression are more likely to binge drink and drink heavily.[12] In this study, the only unhealthy behavior that could be identified was smoking status. Also, possible anti-depressant use was not able to be measured since the HOS survey contains no questions regarding history of anti-depressant use. The pain and depression relationship in this study could be affected by anti-depressant use which is understandably strongly associated with depression.[36]

Also, this dataset contained no ability to measure social involvement to estimate the effect of "connectedness" with family and peers upon risk of depression. Recent research shows that such connectedness may reduce risk of depression in older adults.[37, 38] This can be coupled with emerging evidence that meaningful engagements from roles, such as social activities and volunteering, can function as a protective factor against depression.[39, 40] Strong familial connectedness may also act as a protector against depression.[41] Future research is needed to explore the myriad ways in which social and familial connectedness might modify the relationship between pain and depression.

Public Health Implications

The booming growth in the older adult population makes the evidence presented in this study of their strong risk of depression in the presence of pain especially relevant. However, this also represents an opportunity for public health to positively improve the lives of millions of older adults by intervening and reducing their risk of suffering from the negative effects of depression and other afflictions resulting from it. Projections estimate that by 2020 depression will be second only to heart disease in its contribution to the global burden of disease as measured by disability-adjusted life years.[42] The booming growth in cohorts of older adults combined with the high health care costs for treatment highlight the need to better understand the many avenues to depression, including pain.[43]

This investigation into the pain and depression relationship demonstrates the need to identify modifiable factors that may help reduce the incidence and severity of depression. Evidence indicates that depression screening alone may not improve depression outcomes; however, depression treatments are still effective.[34] The development of interventions for older adults must consider the influence of other chronic conditions, functional impairments, and other comorbidities. One example is how treatment of depression in older adults with arthritis reduces depressive symptoms, as well as improves pain and functional outcomes.[44] Other studies have identified successful depression interventions for older adults and recommend such interventions as depression care management and individual cognitive therapy.[45, 46, 47] The ability to effectively measure risk of depression in the presence of pain while

accounting for other influences will enhance the ability of care providers and public health professionals to more accurately identify older adults at risk of developing subsyndromal and major depression and implement interventions to reduce their risk.

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