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## The association of comorbid conditions with patient-reported outcomes in Veterans with hip and knee osteoarthritis

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## Abstract

There is limited understanding of how comorbid health conditions affect osteoarthritis (OA)-related outcomes. This study examined associations of different comorbidity measures with baseline OA-related patient-reported outcomes (PROs) among patients with hip and knee OA. Data were from patients ( $N=300$ , 9 % female, mean age = 61.1;  $SD=9.2$ ) enrolled in a randomized control trial at the Durham Veterans Affairs Medical Center. Separate multivariable regression models, adjusted for demographic and clinical characteristics, examined the association of each comorbidity measure with baseline PROs: pain, physical function, depressive symptoms, fatigue, and insomnia. Comorbidity measures included the Self-Administered Comorbidity Questionnaire (SACQ), conditions reported as activity-limiting (SACQ-AL), and indicators of depression, diabetes, hypertension, and back pain. Mean (SD) numbers of comorbid conditions and activity-limiting conditions were 3.4 (1.8) and 1.6 (1.4), respectively. Comorbidity scores (SACQ overall and SACQ-AL) and individual comorbidity conditions were each associated with worse OA-related PROs adjusting for demographic and clinical factors. Worse SACQ overall and SACQ-AL scores were associated with worse mean scores for pain, depressive symptoms, fatigue, and insomnia ( $p$  values  $<0.01$ ). Additionally, increasing SACQ-AL scores were associated with worse mean scores for function ( $p<0.01$ ). Depression was associated with worse pain ( $p=0.03$ ), fatigue, and insomnia ( $p$  values  $<0.01$ ). Diabetes was associated with worse fatigue ( $p=0.01$ ), depressive symptoms ( $p=0.02$ ), and insomnia ( $p=0.03$ ). Back pain was associated with worse pain scores ( $p=0.02$ ). Results provide evidence that comorbidity burden, particularly activity-limiting conditions, is associated with worse OA-related PROs. Interventions for patients with OA need to address comorbid conditions and their impact on key outcomes.

## Keywords

Chronic disease; Comorbidity; Osteoarthritis; United States Department of Veterans Affairs

## Introduction

As a result of the increasing prevalence of osteoarthritis (OA) [1] and physical toll placed on individuals' health, OA contributes significantly to societal health care costs [2–4]. To better understand the burden of OA, it is important to contextualize OA relative to other comorbid health conditions that patients may face. Comorbid conditions may exacerbate the symptoms

of OA (e.g., pain and physical limitations) and complicate or even compromise its management. This is particularly important given the high prevalence of multiple comorbid health conditions among individuals with OA [5–7]. For example, in a sample of Medicare enrollees with OA who underwent elective joint replacement surgery, Perruccio and colleagues identified that 68 % of patients with OA reported at least one other comorbid health condition, while nearly 10 % of patients reported three or more other comorbid health conditions [8, 9]. In a community-based cohort of patients with symptomatic knee OA, the average number of additional self-reported comorbid health conditions was 1.73 [10].

Although we know that comorbid conditions are common among patients with OA, little is known about the specific impact of comorbidities on patients' experiences, including their perception of pain, function, insomnia, and depression and fatigue. For example, it is not known whether a cumulative number of chronic health conditions or certain specific health problems may have a stronger negative influence on OA-related patient-reported outcomes (PROs). Understanding these associations can guide clinical care by identifying aspects of comorbidity that have the greatest impact on OA-related PROs and therefore should be emphasized in treatment and care models.

Our objective was to examine associations of both global comorbidity scores and individual chronic conditions with baseline OA-related PROs among patients with hip and knee OA enrolled in an RCT. Most comorbidity scores involve a count of health conditions, some including weights related to risk of outcomes such as mortality or hospitalization [11, 12]. However, these measures typically do not consider the severity of comorbidities in terms of their functional impact, which is of high relevance for patients with OA who already have a functionally limiting condition. We used the Self-Administered Comorbidity Questionnaire, which allows a separate count of conditions that patients report as being “activity-limiting.” This is a novel aspect of this study, as we were able to differentiate between the general burden of comorbid conditions and that of activity-limiting conditions. In addition to global measures of comorbidity, we examined associations of the most common specific comorbid health conditions on OA-related PROs. The goal of this study was to provide a comprehensive evaluation of comorbidity in patients with knee and hip OA, relative to key PROs: pain, physical function, fatigue, insomnia, and depressive symptoms.

## Methods

### Study design and setting

The study uses baseline assessments from a randomized controlled trial of Patient and Provider Interventions for Managing Osteoarthritis in Primary Care, conducted at the Veterans Affairs (VA) Medical Center in Durham, NC, and its associated community-based outpatient clinics. Full details of the study design have been previously described [13]. In brief, this study used a cluster randomized controlled trial design. Thirty primary care providers (PCPs) were randomized to either the intervention or control group. We aimed to enroll ten patients (five white and five non-white) with knee and/or hip OA from each PCP. The provider component of the intervention involved provision of patient-specific treatment recommendations for OA at the point of care. The patient intervention involved 12 months of telephone-based support for key behavioral strategies including weight management,

physical activity, and cognitive behavioral pain management skills. The Institutional Review Board at the Durham Veterans Affairs Medical System approved this study ([clinicaltrials.gov](https://clinicaltrials.gov) tracking number NCT01130740).

## Participants

Eligible patients (1) were receiving care from a participating PCP, (2) had hip OA (based on radiographic evidence in the electronic medical record) and/or knee OA (based on radiographic evidence in the electronic medical record or meeting American College of Rheumatology clinical criteria [14]), and (3) had current symptoms in joint(s) with OA. Participants were overweight (body mass index (BMI)  $\geq 25$ ) and not meeting physical activity guidelines set forth by the Department of Health and Human Services [15]. These guidelines recommend 2 h and 30 min of moderate-intensity or 1 h and 15 min of vigorous-intensity aerobic activity plus two or more sessions of muscle strengthening exercises. As previously reported [13], after an initial electronic eligibility screening, we then further examine the medical record to confirm the presence of an OA diagnosis and scan for exclusion criteria. This is followed about 1–2 weeks later by a screening telephone call to further assess eligibility, with particular focus on criteria that may not appear in the electronic medical record. Patients were excluded based on the presence of specific comorbid conditions, including the following: rheumatoid arthritis, fibromyalgia, or other systemic rheumatic disease; history of gout in knee or hip; hospitalization for a stroke, myocardial infarction, heart failure, or coronary artery revascularization in the past 3 months; severe neurological conditions; Paget's disease; dementia or other memory loss condition; metastatic cancer; referral for hospice or palliative care; serious psychological conditions; current, uncontrolled substance abuse disorder; severely impaired hearing or speech; and blindness.

## Outcome measures

We selected the following five OA-related PROs, assessed at baseline, because of their high relevance to hip and knee OA: pain, physical function, depressive symptoms, fatigue, and insomnia. Pain and physical function limitations are hallmark symptoms of both hip and knee OA and common treatment targets. Both pain and physical function were measured with Likert-summed subscales of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [16]. The WOMAC pain and physical function subscales include 5 and 17 items (ranging from 0 to 4 points each), respectively, with lower summed scores indicating better outcomes [17]. The WOMAC subscales are valid, sensitive measures for pain and function among people with OA [18].

Among people with OA, concomitant depressive symptoms occur frequently and may negatively impact quality of life [19]. Depressive symptoms were assessed with the Patient Health Questionnaire-8 (PHQ-8), a valid and reliable measure that consists of items corresponding to depression criteria listed in the Diagnostic and Statistics Manual Fourth Edition. All items are scored from 0 (not at all) to 3 (nearly every day), resulting in a summed score ranging from 0 to 24 [20]. Patients with OA have a notable amount of fatigue that can impact activity and physical function [21]. Another research suggests that fatigue tends to be more severe as the number of comorbid conditions increases [21]. We assessed

fatigue with a 10-cm visual analog scale that asked patients to indicate how severely fatigue had been a problem for them over the past week, using anchors of “no problem” to “major problem.” At least half of the patients with OA report sleep disturbances [22, 23], making sleep another key PRO in this group of patients. We measured global perceived insomnia symptoms with the Insomnia Severity Index, which includes seven items measured on 5-point Likert scales, for a total range of 0–28.

### Comorbidity measures

We examined six self-reported comorbidity measures. First, we examined the Self-Administered Comorbidity Questionnaire (SACQ), which asks patients to indicate the following about each of 13 health problems and any “other” reported health problems: (1) whether they have the condition (yes/no), (2) whether they receive treatment for the condition (yes/no), and (3) whether the condition limits their activities (yes/no) [24]. Because all participants in this study had OA and rheumatoid arthritis was an exclusion condition, these two conditions were removed from the scoring of this scale in these analyses. This resulted in a possible score range of 0–42 (1 point each for prevalence, treatment, and activity limitation of 11 prespecified conditions plus three possible “other” conditions indicated by the participant). In the development study for the SACQ, test-retest reliability was 0.94 (95 % confidence interval 0.72, 0.99) as calculated by the intraclass correlation coefficient and 0.81 by the Spearman correlation coefficient [24]. Second, since we were particularly interested in activity-limiting health problems, we created a score from the SACQ that summed the number of conditions participants indicated as activity-limiting (SACQAL), again excluding the two arthritis conditions. The possible score range for this scale was 0–14. Third, we were interested in the individual associations of specific health conditions with OA-related PROs. We included the four most common self-reported comorbid conditions on the SACQ, each endorsed by 20 % of participants: depression, diabetes, hypertension, and back pain. These conditions have also been previously shown to commonly co-occur with OA [18, 19, 25, 26].

### Covariates

We included the following demographic and clinical characteristics as covariates because each has been associated with worsened OA experience [5, 10, 18]: age (continuous), race (white vs. non-white, binary), gender (male vs. female, binary), marital status (married or living with partner vs. not married, binary), financial status (live comfortably/meet basic expenses vs. just meet basic expenses/do not have enough, binary), BMI (continuous), number of joints with arthritis symptoms (ordinal), and duration of arthritis symptoms (ordinal).

### Statistical analyses

Since all OA-related PROs were continuous variables, multivariable linear regression models were used to examine the association between each combination of OA-related PRO and comorbidity index or specific comorbid condition. Because comorbid depression (independent variable) and depressive symptoms (dependent variable) measure similar constructs, we did not fit the model for this combination. Each multivariable model included one comorbidity measure and a PRO outcome, as well as the covariates described above.

Residual plots from models were examined to assess normality assumptions. Statistical significance was assessed at a conventional alpha level of 0.05. Data management and analyses were conducted in SAS version 9.2 (SAS Institute, Cary, NC).

## Results

Among 1,433 patients who were approached via letter regarding study participation, 563 were ineligible, 570 declined participation, and 300 consented and completed baseline assessments. Participant characteristics are shown in Table 1. Most patients were men (91 %) since this was a sample of VA health care users. On average, patients experienced arthritis in six joints (SD=3.6) for a mean duration of 14 years (SD=11.6). The mean SACQ score was 7.2 (SD=4.1) with participants reporting means of 3.4 comorbid conditions (SD=1.8) and 1.6 activity-limiting conditions (SD=1.4). Very few patients reported no comorbid conditions ( $n=5$ , 1.8 %), 12.3 % ( $n=34$ ) reported one comorbid condition, 19.6 % reported two comorbid conditions ( $n=54$ ), 23.2 % reported three comorbid conditions ( $n=64$ ), and 43.1 % reported four or more comorbid conditions ( $n=119$ ). We were unable to calculate the SACQ score on 24 patients due to missing data. On the SACQ-AL, 22.5 % of patients reported no activity-limiting comorbid conditions ( $n=66$ ), 32.3 % reported one activity-limiting comorbid condition ( $n=95$ ), 22.8 % reported two activity-limiting comorbid conditions ( $n=67$ ), 11.9 % reported three activity-limiting conditions ( $n=35$ ), and 10.5 % reported four or more activity-limited comorbid conditions ( $n=31$ ). The most commonly reported comorbid conditions were back pain (75 %), hypertension (73 %), depression (39 %), and diabetes (38 %). The proportions of patients who reported these conditions as activity-limiting were as follows: back pain (63 %), hypertension (14 %), depression (26 %), and diabetes (16 %).

We found that comorbidity scores (SACQ overall and SACQ-AL) were associated with worse OA-related PROs adjusting for demographic and clinical factors (Table 2). Increasing (worse) overall comorbidity score (SACQ) was associated with worse mean scores (higher) for four PROs: pain, depressive symptoms, fatigue, and insomnia (Table 2). For example, each 1-point increase in mean SACQ score is associated with an estimated increase of 0.2 point in mean WOMAC pain scores. Increasing SACQ-AL score was associated with worse mean scores (higher) for all PROs: pain, physical function, depressive symptoms, fatigue, and insomnia (Table 2). For example, each 1-point increase in mean SACQ-AL scores is associated with an estimated increase of 0.7 point in mean WOMAC pain scores.

We also found that individual comorbidities were associated with worse OA-related PROs adjusting for demographic and clinical factors (Table 2). Specifically, participants with comorbid depression had higher mean (worse) scores than those not having depression for three PROs: pain, fatigue, and insomnia. For example, participants with comorbid depression had an estimated 1 point higher mean WOMAC pain score than those who did not have depression. Participants with diabetes had higher mean (worse) scores than those not having diabetes for three PROs: fatigue, depressive symptoms, and insomnia. Participants with back pain had an estimated 1.2 point higher mean WOMAC pain score than those without back pain. We found no significant associations between hypertension and any PROs.

For the covariates included in each model along with the comorbidity measures, in general, we found similar associations across models for the same PRO. Age, BMI, and duration of arthritis symptoms were associated with WOMAC pain in all comorbidity models. Race and financial status were additionally associated with WOMAC pain in models for the comorbidity summary scores (e.g., SACQ and SACQ-AL). Race, financial status, BMI, and the number of joints with arthritis symptoms were associated with WOMAC physical function in all comorbidity models. For the PRO depressive symptoms, age, marital status, financial status, and the number of joints with arthritis symptoms were associated in all models. Age, financial status, and BMI were generally associated with the PRO of fatigue. For the insomnia PRO, age and race were associated in all models; in addition, financial status and the number of joints with arthritis symptoms were associated in most models.

## Discussion

Patients with OA often suffer from other comorbid conditions, adding to the complexity of their health care needs. In this study sample, patients reported an average of 3.4 additional comorbid conditions. Generally consistent with analyses conducted outside of the VA health care system [9], we found that approximately one third of patients reported one or two comorbid conditions and almost half reported three or more comorbid conditions. We also specifically evaluated self-reported activity-limiting comorbidities; patients reported an average of 1.6 of these conditions, with 22 % reporting three or more comorbid activity-limiting conditions additional to OA. This high number of comorbid activity-limiting conditions is particularly striking since lower extremity OA itself limits activities for many patients. These data highlight the importance of assessing functional limitations among patients with hip and knee OA, not only simply related to their OA but also to comorbid conditions.

This study confirmed that comorbid conditions are associated with worse scores on a wide range of PROs relevant to lower extremity OA. Although per-unit changes in PRO scores were small to moderate for each unit change in comorbidity indices, many patients with OA have multiple comorbid conditions that cumulatively can have a substantial impact on PROs. It is particularly noteworthy that associations with PROs were strongest for the total number of activity-limiting comorbid conditions (SACQ-AL), which was significantly associated with all PROs: pain, decreased physical function, depressive symptoms, fatigue, and insomnia. These results emphasize the importance of screening for and addressing other severe health problems that limit patients' activities. Physical activity and rehabilitation interventions can be important tools for addressing activity limitations due to both OA and comorbid conditions. However, these interventions are currently underutilized in patients with OA [27]. Our results suggest that use of these types of interventions should be emphasized for patients with OA and comorbid activity-limiting health problems, who are at greatest risk for worse PROs. In addition to associations of overall comorbidity with PROs, we found associations for common individual comorbid health conditions, particularly depression, diabetes, and back pain. Diabetes and depression were each associated with three PROs, confirming their impact across multiple health domains [19, 28].

There are opportunities to make meaningful changes in the lives of patients with OA by recognizing patients' comorbid conditions and enabling self-management. These study results emphasize that several health conditions (diabetes, depression, and back pain) appear to have an additional impact on health outcomes already affected by lower extremity OA (e.g., pain, fatigue, insomnia, and depressive symptoms). These results emphasize the importance of chronic care models that consider the combined impact and effective management strategies for these frequently co-occurring conditions. Efficiently identifying patients with multiple comorbid conditions has the potential to mitigate the potential negative impact of comorbid conditions on patients' health and subsequently reduce health care utilization and cost. Such programs could intensively manage, for example, diabetes or depression, in parallel with OA management, or alternatively could increase the intensity and support of the OA-specific management in patients with comorbidities.

Our study had several limitations. Some of the associations between comorbid conditions and PROs may be endogenous. For example, it is uncertain whether diabetes causes patients to experience negative PROs such as physical limitations and depression or whether physical limitations and depression predispose patients to behavioral risk factors for diabetes. Our sample originated from a single Veterans Affairs medical center. It is possible that patients seeking care in the Veterans Affairs health care system have higher severity of illness [29] than their counterparts seeking care in the private sector. We assert that this limitation has minimal implications as our results are similar to those identified in non-federal health systems [10]. The Veteran population is predominately male, as is this study population, yet osteoarthritis is more prevalent among females [30]. While we controlled for gender in statistical models, this gender difference may limit the generalizability of study findings. We did not obtain de novo radiographs in this pragmatic trial; although radiographic changes are not highly correlated with symptoms, this degree of structural change may certainly impact pain and other PROs, and therefore, this may be a limitation. Lastly, this study used patient self-report data. While patient self-report data has value because it is from the patients' perspective, it is possible that patients did not accurately report their comorbid conditions. This is a limitation to all self-report comorbidity measures, and the SACQ has shown adequate associations with chart abstraction [24]. In addition, perceptions of whether or not a condition is activity-limiting may differ by individual.

## Conclusion

Patients with OA face a multitude of comorbid conditions, such as depression, diabetes, and back pain, which they must manage in addition to OA. More research is needed to understand the intricate interplay of comorbid conditions and their impact on patients with OA. There is a need for clinical care models and other interventions that simultaneously address the complexity and interrelationships of multiple chronic health conditions in the context of OA.

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**Table 1**Baseline patient characteristics ( $n=300$ )

Demographic characteristics	<i>N</i> (%)
Mean age in years (SD)	61.1 (9.2)
Male	272 (90.7)
Race	
White	150 (50.0)
Non-white	150 (50.0)
Married/living with partner	199 (66.3)
Greater than high school education (graduate or GED)	219 (73.0)
Employed or student	127 (42.8)
Disabled	98 (33.0)
Adequate financial status	197 (65.7)
Physical characteristics	
Mean body mass index (SD)	33.8 (5.8)
Mean number of arthritic joints (SD)	6.2 (3.6)
Mean duration of arthritis systems in years (SD)	14.2 (11.6)
Comorbid conditions	
Depression	118 (39.3)
Diabetes	114 (38.0)
Hypertension	219 (73.0)
Back pain	226 (75.3)
Comorbidity summary scores	
Comorbidity summary score (SACQ) (mean (SD))	7.2 (4.1)
Activity-limiting summary score (SACQ-AL) (mean (SD))	1.6 (1.4)
Patient-reported outcomes (mean (SD))	
Pain (WOMAC)	10.2 (4.0)
Physical function (WOMAC)	33.8 (13.0)
Depressive symptoms (PHQ-8)	6.8 (5.4)
Fatigue (visual analog scale)	4.8 (3.2)
Insomnia (ISI)	11.4 (8.0)

Data were missing for several variables: duration of arthritis symptoms (missing  $n=1$ ), comorbid depression ( $n=3$ ), hypertension ( $n=3$ ), back pain ( $n=1$ ), SACQ score ( $n=31$ ), SACQ-AL score ( $n=6$ ), pain (WOMAC) ( $n=1$ ), physical function (WOMAC) ( $n=1$ ), depressive symptoms (PHQ-8) ( $n=4$ ), and insomnia (ISI) ( $n=2$ )

**Table 2**

Results of multivariable regression models examining the association between each combination of comorbidity measures (SACQ and SACQAL) and individual comorbidity conditions and OA-related patient-reported outcomes adjusted for demographic and clinical factors ( $n=300$ )

	Pain			Physical function			Depressive symptoms			Fatigue			Insomnia		
	$\hat{B}$	95 % CI	<i>p</i>	$\hat{B}$	95 % CI	<i>p</i>	$\hat{B}$	95 % CI	<i>p</i>	$\hat{B}$	95 % CI	<i>p</i>	$\hat{B}$	95 % CI	<i>p</i>
SACQ	0.2	0.0-0.3	0.008	0.3	-0.0-0.7	0.086	0.4	0.3-0.6	<0.001	0.2	0.1-0.3	<0.001	0.6	0.4-0.8	<0.001
Activity-limiting	0.7	0.4-1.0	<0.001	2.1	1.1-3.2	<0.001	1.4	1.0-1.8	<0.001	0.7	0.4-0.9	<0.001	1.8	1.2-2.4	<0.001
Depression	1.0	0.1-1.9	0.025	1.8	-1.1-4.8	0.223	5.5	4.4-6.5	<0.001	1.6	0.9-2.3	<0.001	5.5	3.8-7.2	<0.001
Diabetes	0.6	-0.3-1.4	0.193	0.9	-1.9-3.8	0.525	1.3	0.2-2.5	0.024	0.9	0.2-1.6	0.015	1.9	0.2-3.7	0.030
Hypertension	0.4	-0.6-1.3	0.437	1.1	-2.1-4.3	0.510	-0.3	-1.6-1.0	0.631	-0.6	-1.4-0.2	0.136	-1.2	-3.2-0.8	0.241
Back pain	1.2	0.2-2.2	0.023	3.0	-0.3-6.3	0.076	1.3	-0.1-2.7	0.062	0.1	-0.7-1.0	0.732	1.6	-0.4-3.7	0.122

All models controlled for patients' age, race, gender, marital status, financial status, BMI, number of arthritic joints, and duration of arthritis. Data were missing for several variables. The number of observations used in the models with the SACQ ranged from 264 to 268, activity-limiting comorbidities ranged from 289 to 293, depression ranged from 292 to 296, diabetes ranged from 295 to 299, hypertension ranged from 292 to 296, and back pain ranged from 294 to 298