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Arthritis Increases the Risk for Fractures---Results from the Women's Health Initiative

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Abstract

Objective—The relationship between arthritis and fracture was examined in the Women's Health Initiative (WHI).

Methods—Women were classified into three self-reported groups at baseline: no arthritis (n=83,295), osteoarthritis (OA) (n=63,402), and rheumatoid arthritis (RA) (n=960). Incident fractures were self-reported throughout follow-up. Age-adjusted fracture rates by arthritis category were generated, and Cox-proportional hazards model was used to test the association between arthritis and fracture.

Results—After an average of 7.80 years, 24,137 total fractures were reported including 2,559 self-reported spinal fractures and 1,698 adjudicated hip fractures. For each fracture type, age-adjusted fracture rates were highest in the RA group and lowest in the non-arthritic group. After adjustment for several covariates, report of arthritis was associated with increased risk for spine, hip, and any clinical fractures. Compared to the non-arthritis group, the risk [HR (95% CI)] of sustaining any clinical fracture in the OA group was 1.09 (1.05, 1.13) ($p<0.001$) and 1.49 (1.26, 1.75) ($p<0.001$) in the RA group. The risk of sustaining a hip fracture was not statistically increased in the OA group [1.11 (0.98, 1.25)] ($p=0.122$) compared to the non-arthritis group; however the risk of hip fracture significantly increased [3.03 (2.03, 4.51)] ($p<0.001$) in the RA group compared to the non-arthritis group.

Conclusion—The increase in fracture risk found in this study confirms the importance of fracture prevention in patients with both RA and OA.

Key Indexing Terms

Arthritis; Epidemiology; Fracture; Postmenopausal Women

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INTRODUCTION

With an increasing number of older adults in our society, osteoporosis has become a major public health concern. Fragility fractures, the most devastating outcome associated with osteoporosis, have been shown to lead to increased pain and disability, decreased quality of life (1), and higher mortality rates (2). Age and bone mineral density (BMD) are the primary risk factors associated with osteoporosis and fragility fractures (3), but others noted in FRAX®, the current World Health Organization fracture assessment calculator, include gender, weight, height, history of fractures, history of parental hip fracture, smoking, alcohol use, history of secondary osteoporosis, glucocorticoid (GC) use, and the presence of certain co-morbid conditions, such as rheumatoid arthritis (RA) (1).

RA is a multi-system inflammatory disorder characterized by inflammation and destruction of synovial joints (4). RA patients have lower BMD's (5–7) and an increased fracture risk compared to non-arthritic controls (8–10). RA affects about 1% of the general population (11), where as osteoarthritis (OA), a commonly used arthritic comparison population in RA studies, affects about 30% of adults; making it the most common arthritic condition.

OA is typically not associated with fractures, and was previously thought of as a "protective" factor for fractures. Studies by Cumming (12), Dequeker (13), and Kanis (14) showed a reduction in fracture risk in OA cases, and studies by Jones (15) and Arden (16) showed no increased or reduced risk in fractures among OA cases. In contrast, Bergink (17) and subsequent study by Arden (18) found an increased risk in their OA cases.

Arthritis, in general, is one of the largest public health concerns for aging populations. In the United States, direct and indirect costs attributable to arthritis and other rheumatic conditions have been estimated to total $128 billion (19), and the number of individuals diagnosed is expected to increase an average of 16% by year 2030 (20). If arthritis, particularly OA, is associated with an increased risk of fractures, then the increasing arthritis prevalence would indicate a potential increase in fracture outcomes and associated complications.

The primary goal of this paper is to investigate fracture risk in a group of multi-ethnic postmenopausal self-reported arthritis cases compared to non-arthritic controls. This paper will also test if the association is modified by ethnicity or GC use.

MATERIALS AND METHODS

The association between arthritis and fracture was evaluated prospectively using data from the Women's Health Initiative (WHI). The exposure, arthritis status, was self-reported by participants at baseline. The outcome, incident fractures, was reported over the follow-up period. All participants gave written consent to participate in the WHI, and the University of Arizona Institutional Review Board approved this current study.

Women's Health Initiative (WHI)

The WHI is a nationwide study that investigated the risk factors and preventive strategies of the major contributors to morbidity and mortality in postmenopausal women from the United States: including heart disease, breast and colorectal cancer, and osteoporotic fractures (21). The WHI recruited 161,808 postmenopausal women aged 50 to 79 years from 40 centers across the country to participate in the clinical trials (CT) component, including the hormone therapy trials (HT), dietary modification trial (DM), and the calcium and vitamin D trial (CaD), or the observational study (OS). Details of recruitment strategies and baseline participant information have been previously published (22).

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Defining arthritis status

The WHI health assessment form was used to identify arthritis status at baseline. The participants were asked, “Did your doctor ever tell you that you have arthritis?” with responses of yes or no. Women responding “yes” were then asked “What type of arthritis do you have?” with responses of “rheumatoid arthritis” and “other/do not know”. For this study, the arthritis exposure variable consists of three categories: 1) non-arthritic control group, including the women who answered “no” to the initial arthritis question; 2) OA group, including those women answering “yes” to the initial arthritis question and answering “other/do not know” on the arthritis type question; and 3) RA group, those women reporting RA as arthritis type plus one of the commonly used rheumatologic treatment medications.

Wright and colleagues previously published that the other/do not know group serves as the proxy for OA (23), and Walitt and colleagues found that the combination of self-report and medication had the highest positive predictive value (62.2%) for defining RA within the WHI compared to self-report alone (24). Women were excluded if they did not respond to the initial or follow-up arthritis question, if they reported RA but did not report one of the treatment medications of interest, or if they reported other rheumatologic or inflammatory arthritic conditions including lupus or ulcerative colitis.

Fracture ascertainment

The participants self-reported clinical fractures during periodic medical updates (every six months for women participating in the CT, and yearly for the women participating in the OS). The WHI collected information on fractures of the upper and lower arm, elbow, spine, tailbone, hip, upper and lower leg, and foot, but excluded fractures of the ribs, sternum, skull or face. All fractures reported in the CT and all hip fracture (CT and OS) were adjudicated by review of radiologic reports or medical records by centrally trained and masked physicians (25). The fractures of interest in this analysis included total (all types of fracture), spine, and hip.

Covariates

Variables associated with arthritis and/or fractures were considered as possible covariates including: age, race/ethnicity, body mass index (BMI), education, income, physical activity, hospitalizations, number of falls in the previous year, smoking status, alcohol use, hormone use status, parental fracture >40 years, calcium and vitamin D intake, depression score, years since menopause, personal fracture after 55 years, joint replacements, general health score, and use of certain medications (phenobarbital, anticonvulsants, anti-Parkinsonian drugs, antidepressants, anti-anxiety drugs, thyroid medicatoions, thiazolidinediones, proton pump inhibitors, thiazide diruetics, statins, bisphosponates, calcitonins, non steroidal anti-inflammatory drugs, estrogens, heparin, and selective-estrogen receptor modulators).

All covariates were assessed at baseline. Height and weight were measured using standardized procedures by WHI clinical staff, and were used to calculate BMI (kg/m^2). Race/ethnicity was classified into 6 categories: American Indian or Alaskan Native, Asian or Pacific Islander, African American, Hispanic/Latino, White (not of Hispanic origin), or other. Women reported highest level of education completed, if they had been hospitalized in the last 2 year (yes or no), fracture at the age of 55 or older (yes or no), and the number of times they fell to the ground in the past 12 months (0, 1, 2, ≥3). Summary variables were generated based on questions regarding parental fractures (yes or no), physical activity (metabolic equivalence units (METs) per week), hormone use (never, past, or current user), smoking status (non, past, or current smoker), and alcohol use (non, past, or current drinker). Years since menopause was calculated based on reported last menstrual period. Questions from the Rand 36-Item Health Survey were used to compute a general health construct, and

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questions from the center for epidemiological studies depression scale (CES-D) were used to calculate a depression score. Dietary calcium and vitamin D amounts generated from food frequency questionnaire data were combined with amounts reported from supplemental use to generate total calcium and vitamin D variables. Binary variables for each class of drugs were used. Bisphosphonates and calcitonin were combined to create an osteoporosis medication summary variable. Variables related to the WHI design, such as clinical trial assignment (not randomized, placebo, or intervention), were also included as covariates.

Statistical analysis

Descriptive statistics by arthritis group were performed using analysis of variance (ANOVA) for continuous variables and chi-squared tests for categorical variables. Age-adjusted fractures rates and 95% confidence intervals (95% CI) by arthritis group were calculated using direct standardization. Cox-proportional hazards models were used to test difference in risk of fracture between groups. Days from randomization to fracture served as the event time, and days from randomization to last contact served as the censoring time for those who did not fracture. Marginal analyses were performed for each covariate, which was included in the full model if the covariate was significant $p<0.2$ at the 0.05 alpha level in a 2-sided test. Backward elimination techniques were used to produce the final model, including all variables statistically ($p<0.05$) or biologically significant. Survival estimates were generated to graphically portray group differences in fracture risk. Ethnicity and GC interactions were tested using cross-product interaction terms (for example arthritis*ethnicity) and stratified analyses. All analyses were performed in STATA v. 10 (Statacorp, College Station, TX).

RESULTS

Of the 161,808 women enrolled in the WHI, 147,657 were not missing arthritis information and did not report lupus or ulcerative colitis. Of that, 83,295 (56.4%) were included in the non-arthritic control group. Of the women who reported arthritis, 63,402 (43.0%) were placed in the OA group, and 960 (0.65%) women met the criteria for the RA group. All other women were excluded from analyses.

Differences in baseline demographic and lifestyle variables were present by arthritis group. The OA and RA groups were significantly older than the non-arthritic control group, with the OA group being on average 2.92 years older (bonferonni p-value <0.001) than the non-arthritic control group, and the RA group being on average 2.86 years older (bonferroni p-value <0.001) than the non-arthritic controls. The arthritis groups had a larger percentage of African Americans compared to the non-arthritic control group (RA: 13.2%, OA: 9.3%, non-arthritic control: 8.2%). In a post-hoc chi-squared test, the percentage of African Americans in the OA was found to be significantly higher in the OA group compared to the non-arthritis group (p<0.001), and similarly the percentage of African Americans in the RA group was significantly higher (p<0.001) than the non-arthritis group, The OA group had the largest mean weight (75.5 kg) followed by the RA group (73.2 kg) and the non-arthritic control group (71.7 kg). The weight of the OA group was significantly higher than the non-arthritis group (bonferroni p-value <0.001) and the RA group (bonferroni p-value <0.001), and the RA weight was significantly higher than the non-arthritis group (bonferroni p-value 0.025). There were statistically significant differences in the percentage of hospitalization the last 2 years (RA: 28.0%,OA: 18.4%, no arthritis: 11.6%) (overall p<0.001) and history of fracture at ≥55 years (RA: 20.0%, OA18.8%, no arthritis14.1%) (overall p<0.001). Complete descriptive information with overall ANOVA and chi-squared test p-values can be found in Tables 1 and 2.

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Fractures in the WHI

As of March 2008, the women were followed for a mean (SD) of 7.80 (1.54) years, and 24,137 clinical fractures of any type; 2,559 fractures of the spine; and 1,698 hip fractures were reported in the study population (Table 3). The age-adjusted rate (95% CI) per 100 person-years for sustaining total fractures (fracture of any type) was 2.11 (2.08, 2.15) in the non-arthritic control group, increasing to 2.51 (2.46, 2.55) in the OA group, and 3.64 (3.17, 4.11) in the RA group (Figure 1). The age-adjusted spine fracture rate increased from 0.19 to 0.26 per 100 person-years between the control group and the OA group, and increased again to 0.50 per 100 person-years in the RA group. There was no difference in hip fracture rates between the control group and the OA group (0.14/100 vs. 0.16/100), but there was an increase in the hip fracture rate in the RA group (0.51/100) (Figure 1).

Testing the association between arthritis and fracture risk

No significant interaction between ethnicity or GC use was found in the association between arthritis and fracture. Covariates included in the final Cox-proportional hazards model included: age, race/ethnicity, BMI, physical activity, assignment in all clinical trials, hospitalizations, number of falls, smoking status, hormone use, parental fracture >age 40, personal fracture ≥55, total calcium & vitamin D intake, depression score, years since menopause, joint replacements, use of diabetic and osteoporosis medications, and general health score. In comparison to the non-arthritic control group, there was a significant risk for sustaining any type of fracture in both the OA [hazard ratio (95% CI)] [1.09 (1.05, 1.13)] and RA groups [1.49 (1.26, 1.75)] (Table 4). In comparison to the non-arthritic control group, the risk of spine fracture was 1.17 (1.05, 1.29) (p=0.004) and 1.93 (1.29, 2.90) (p= 0.001) in OA and RA groups, respectively (Table 4). No significant increase in hip fracture risk was observed in the OA group [1.11 (0.98, 1.25)] compared to the non-arthritic control group; however, a highly significant increase in hip fracture risk [3.03 (2.03, 4.51)] was observed in the RA group compared to the non-arthritic control group (Table 4).

DISCUSSION

In this large population of postmenopausal women, self-reported arthritis is associated with significant fracture risk increase in women reporting OA and RA. After controlling for several covariates, the RA group had a highly significant increased risk of all fractures studied (HR_{total} = 1.49, HR_{spine} = 1.93, HR_{hip} = 3.03) in comparison to the non-arthritis group. Modest significant increases in total (HR = 1.09) and spine (HR = 1.17) fracture risk were seen in the OA group in comparison to the non-arthritis group, but no significant increase in hip fracture risk was seen. The associations found between arthritis and fracture were not modified by race, ethnicity, or glucocorticoids use in this study.

The RA findings from this study are consistent with the literature showing an increased risk of fractures in RA patients (9, 10, 26). Recently, incidence of any, spine and hip fracture in the Consortium of Rheumatology Researchers of North American (CORRONA) Registry were reported to be 3.71, 0.78, and 0.66 per 100 person-years, respectively (27). The age-adjusted fracture rates for the RA group were 3.64, 0.49, and 0.50 per 100 person-years for total, spine, and hip fracture in the WHI, and though the CORRONA registry includes premenopausal women and men, the incidence rates of the nationwide CORRONA registry are comparable to the rates found in the WHI.

General lifestyle and demographic osteoporosis risk factors, such as age, smoking, and physical activity, play a significant role in fracture risk (1), but the primary risk factor for fracture is low BMD. It has been well documented that RA patients have lower BMD at many skeletal sites compared to various control populations (6, 7, 28), and though BMD was

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not examined in this study, it is highly probable that the associations seen are in part, driven by BMD. A sensitivity analysis in the participants from three WHI clinical centers with available BMD measurements was proposed, however, could not be adequately completed due to the low frequency of fractures (total fractures n=22; spine fractures n=2; hip fractures n=3) in the smaller RA group (n=78).

The risk of sustaining any clinical fracture and a spinal fracture was modestly but significantly increased in the OA group compared to the non-arthritic controls. It is likely that the effects of OA on fracture rate are being underestimated in this study due to the misclassification inherent in self-reporting OA. As previously mentioned, the association between OA and fracture has been mixed in the literature. The most recent study to suggest OA increases the risk of fractures reported by Arden and colleagues found that after adjusting for falls and the use of walking aids, clinician diagnosed knee OA patients had a significant risk for non-vertebral fractures [1.48 (1.00, 2.19)], and no significant association was seen between clinician diagnosed knee OA patients and risk for hip fracture [1.84 (0.78, 4.34)] (18). Though the results of our study are in agreement with the Arden study, the use of clinically diagnosed, site-specific OA patients yielded higher fracture estimates than those found in our study using self-reported OA cases.

In contrast, the most recent study showing a protective effect of OA on fracture risk was a case-control population-based study conducted in Denmark. After adjustment for several variables, Vestergaard and colleagues found an significant risk reduction for any fracture, hip, and spine fractures in participants with OA duration greater than two years (29). Population demographics could be the primary explanation for the difference associations seen between the Vestergaard study and the current, as the Danish population used was almost 20 years younger than the WHI population.

Though a consensus has not been reached, several biological mechanisms have been proposed relating OA to fracture. Like RA, the increase in fracture in OA patients could be driven through a BMD pathway. Studies have shown that BMD in OA populations is typically higher than non-arthritic populations (30–32); therefore, this argument does not provide a good explanation for increases in fracture. Though OA patients have a higher BMD or bone quantity, quality or strength of the bones may be compromised compared to other arthritic and non-arthritic populations. Javaid and colleagues assessed hip structural geometry, as a marker of bone strength, in a group of OA patients and found alterations in geometry precede OA diagnosis (33), suggesting a biological process involved in OA potentially alters bone strength.

Falling is another proposed OA fracture mechanism. OA, especially at sites like the knee and hip, is associated with increased pain, decreased postural stability, and decreased muscle strength, all which have been shown to be significant contributors to fall risk (34–36). Falling is a well-documented risk factor for fractures (1), and early studies have shown that the self-report of OA is associated with increased risk of falls (37, 38). More recently, Foley and colleagues did not see increased risk for falls in knee and hip radiographic OA cases, but did see that report of pain is highly associated with falls and OA patients reported more pain (39).

One last possibility is that our results represent the consequences related to behavioral and physiologic changes that occur in individuals that perceive articular discomfort they classify as arthritis. Self-reported health status has been shown to be an independent risk factor for fractures in many studies (40–44). It is possible that self-reported arthritis in the WHI is a measure of autoperception that encompasses a variety of health domains, such as pain, balance confidence, self-efficacy, and functional status.

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Strengths and limitations

This study has several limitations related to the arthritis exposure. Regarding OA, the limitations associated with self-report and the use of a proxy measure of OA within the WHI previously described by Wright and colleagues apply to this analysis (23). Walitt and colleagues also found that self-reported OA in the WHI was very sensitive (95.0%), but not particularly specific (23.4%), and only had fair agreement between self-reported OA and chart review (kappa = 0.23) (unpublished data). The potential for the moderate amount of misclassification in the OA group would bias the results of this study to the null. People experiencing joint pain due to a previous injury, have other soft-tissue condition such as tendonitis, or other non-inflammatory arthritic conditions, may report having OA though not clinically diagnosed. This could also lead to a moderate amount of misclassification, again, biasing the estimates towards the null. Not having site specific or radiographically confirmed OA cases is another limitation of this study. Fracture risk is probably different for persons with OA of the hip compared to persons with knee, hand, or spine OA. The OA affected area may have a higher BMD, whereas regions without OA have normal or low BMD, potentially altering overall fracture risk.

Regarding the RA classification, the use of medication in the RA definition probably captured true RA cases, but these may represent the more severe cases, potentially overestimating the effect of RA on fracture risk. This study did not take into account incident cases of arthritis and the effect it has on fracture risk, and it also did not also account for the additive or multiplicative effect of having both conditions on fracture risk.

The use of self-reported fracture outcomes can also be seen as a limitation. Sensitivity analyses were performed using adjudicated fractures only. Slight changes in the point estimates were observed with the smaller sample size, however, the overall conclusions did not change. Chen and colleagues found high agreement between self-report and adjudicated fractures in WHI sub-study (45), assuring high quality of the fracture data used in this study.

This study adjusted for several covariates, but was unable to adjust for GC use, as it was used in the definition of the RA group. To test the possible interaction of GCs in the relationship between arthritis and fracture, a categorical variable was created capturing users and non-users in each arthritis group (data not shown). Though no interaction was present, the point estimate of the fracture risk was higher in GC users compared to non-users, and by not adjusting for GCs, the true fracture risk for women not taking GCs was overestimated and the risk was underestimated for women using GCs.

Though limited by the above mentioned factors, there are many strengths of the study. The most notable is the size of the WHI, and the size of each of the exposure groups. Having over 63,000 women in the OA group gave more than adequate power to estimate the effects OA have on fracture outcomes. Though not clinically ascertained, the prevalence of OA in the WHI population was approximately 43%, which is comparable to the 42% prevalence of radiographic OA in the hands, knees, and hips found in the women 60 years and older participating in National Health and Nutrition Examination Survey (NHANES)-III (46). The OA limitations presented would have resulted in estimates being biased toward the null; however, significant association remained in our study. Though not reaching general population prevalence estimates, the RA group sample size was large enough to confirm the association between RA and fracture. The WHI also had a larger percentage of women from minority groups, which allowed for examination of effect modification by race and ethnicity. The women of the WHI were followed on average almost 8 years, ensuring adequate numbers of fracture outcomes, especially for the more rare hip fracture outcome.

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Conclusions

Arthritis and osteoporosis are import public health conditions for older adults. OA and RA affect over 25 million adults in the United States and fractures costs billions of health care dollars annually. The increase in fracture risk found in this study confirms the importance of fracture prevention in both patients with RA and OA.

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Appendix

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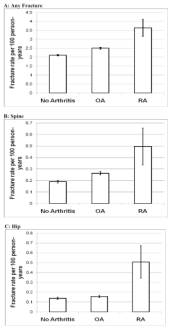

Figure 1.

Age-Adjusted Fracture Rates by Arthritis Status

Age-adjusted rates per 100 person-years and 95% confidence intervals (A) Any Fracture; (B) Spine; (C) Hip

OA: Osteoarthritis

RA: Rheumatoid arthritis

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Table 1

Baseline Characteristics of Categorical Variables by Arthritis Status

	No Arthritis* (n=83,295)		OA* (n=63,402)		RA* (n=960)	
	N	%	N	%	N	%
Baseline Age Group						
50–59	33,804	40.58	15,378	24.25	240	25.00
60–69	35,446	42.55	30,248	47.71	448	46.67
70–79	14,045	16.86	17,776	28.04	272	28.33
Race/Ethnicity						
White	68,699	82.68	53,153	84.05	741	77.35
Hispanic	3,573	4.30	2,060	3.26	38	3.97
African American	6,817	8.20	5,857	9.26	126	13.15
Asian	2,721	3.28	1,191	1.88	26	2.71
American Indian	317	0.38	292	0.46	9	0.94
Unknown	967	1.16	686	1.09	18	1.88
Hormone Trial						
Not randomized	68,819	82.62	53,487	84.36	878	91.46
Intervention	7,374	8.85	4,887	7.71	41	4.27
Control	7,102	8.53	5,028	7.93	41	4.27
Dietary Modification Trial						
Not randomized	57,310	68.80	45,779	72.20	812	84.58
Intervention	10,398	12.48	7,069	11.15	59	6.15
Control	15,587	18.71	10,554	16.65	89	9.27
Calcium and Vitamin D Trial						
Not randomized	63,522	76.26	50,503	79.66	866	90.21
Intervention	9,906	11.89	6,434	10.15	53	5.52
Control	9,867	11.85	6,465	10.20	41	4.27
Hospitalized in Last 2 Years						
No	69,909	88.43	51,453	81.59	683	72.05
Yes	9,143	11.57	11,607	18.41	265	27.95
Number of Falls in 12 Months						

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	No Arthritis* (n=83,295)		OA* (n=63,402)		RA* (n=960)	
	N	%	N	%	N	%
0	57,007	71.34	40,530	64.10	612	64.15
1	15,054	18.84	13,331	21.08	201	21.07
2	5,454	6.83	6,123	9.68	97	10.17
3+	2,398	3.00	3,248	5.14	44	4.61
Parental Fracture >40 Years						
No	47,303	61.00	34,447	59.34	547	62.37
Yes	30,242	39.00	23,605	40.66	330	37.63
Fracture at Age 55+						
No	52,476	85.93	43,140	81.24	631	80.08
Yes	8,595	14.07	9,961	18.76	157	19.92
Smoking Status						
Never smoked	42,597	51.69	31,502	50.34	437	46.00
Past smoker	33,770	40.98	27,124	43.35	443	46.63
Current smoker	6,046	7.34	3,947	6.31	70	7.37
Hormone Therapy Use						
Never used	37,413	44.95	26,774	42.27	397	41.40
Past user	12,221	14.68	10,979	17.33	161	16.79
Current user	33,593	40.36	25,589	40.40	401	41.81
Osteoporosis Medications Use						
No	81,787	98.19	61,653	97.24	892	92.92
Yes	1,508	1.81	1,749	2.76	68	7.08
Thiazolidinediones Use						
No	83,240	99.93	63,339	99.90	958	99.79
Yes	55	0.07	63	0.10	2	0.21
Previous Joint Replacement						
No	77,918	99.20	58,604	93.29	773	81.28
Yes	628	0.80	4,218	6.71	178	18.72

OA: Osteoarthritis
RA: Rheumatoid arthritis

*all variables significantly different between the three groups at p<0.001, with the exception of thiazolidinediones (p=0.020)

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Table 2

Baseline Characteristics of Continuous Variables by Arthritis Status

	No Arthritis* (n=83,295)		OA * (n=63,402)		RA* (n=960)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (yrs)	61.89	7.14	64.81	7.01	64.75	7.12
Height (cm)	162.00	6.58	161.50	6.73	161.10	6.76
Weight (kg)	71.74	15.94	75.45	17.71	73.18	17.78
Body Mass Index (kg/m^2)	27.19	5.49	28.78	6.28	28.10	6.40
Years Since Menopause	13.60	9.36	16.90	9.62	16.71	9.97
Total Calcium Intake (mg)	1,148.00	750.00	1,207	734.10	1,264.00	837.60
Total Vitamin D Intake (mg)	8.92	6.87	9.66	7.12	9.88	6.84
CES-D Depression Score	0.03	0.11	0.05	0.14	0.05	0.14
Total Physical Activity per Week (METS)	13.35	14.34	11.53	12.92	9.58	11.46
General Health Construct	78.52	16.00	70.03	18.07	57.26	20.35

OA: Osteoarthritis
RA: Rheumatoid arthritis

* All variables significantly different between the three groups at $P<0.001$

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Table 3

Frequency of Fracture in the WHI and by Arthritis Status

	No Arthritis (n = 83,295)		OA (n = 63,402)		RA (n = 960)			Total Population (n = 147,657)	
	N	%	N	%	N	%	p-value	N	%
Any Fracture	12,411	14.9	11,488	18.1	238	24.8	<0.001	24,137	16.3
Spine	1,126	1.4	1,395	2.2	38	4.0	<0.001	2,559	1.7
Hip	775	0.9	885	1.4	38	4.0	<0.001	1,698	1.1

OA: Osteoarthritis
RA: Rheumatoid arthritis

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Table 4

The Risk of Fracture by Arthritis Group

	No Arthritis (n=83,295)	OA (n=63,402)		RA (n=960)	
		HR (95% CI)	p-value	HR (95% CI)	p-value
Any Fracture (n=24,137)	Ref.	1.09 (1.05, 1.13)	<0.001	1.49 (1.26, 1.75)	<0.001
Spine (n=2,559)	Ref.	1.17 (1.05, 1.29)	0.004	1.93 (1.29, 2.90)	0.001
Hip (n=1,698)	Ref.	1.11 (0.98, 1.25)	0.105	3.03 (2.03, 4.51)	<0.001

* Adjusted for age; race; BMI; physical activity; assignment in the HT trial, DM trial, and CaD trial; hospitalizations; falls; smoking ; hormone use; parental fracture >age 40; calcium & vitamin D intake; depression score; years since menopause; diabetic treatments; osteoporosis medication; general health score; fracture >55; and joint replacements

OA: Osteoarthritis
RA: Rheumatoid arthritis