A description of patient- and rheumatologist-reported depression symptoms in an American rheumatoid arthritis registry population

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Abstract

Objective

Depression is a common and important comorbidity in patients with rheumatoid arthritis (RA). The study aim was to describe rates of depressive symptoms and their associations with RA disease activity using measures reported from patients and rheumatologists.

Methods

The Consortium of Rheumatology Researchers of North America (CORRONA) registry is an observational cohort with data on more than 33,000 RA patients. Using depression symptom measures reported separately by patients and rheumatologists, lifetime prevalence, 12-month prevalence, and annualised incidence rates (IR) were estimated. Additionally, cross-sectional associations between RA disease and a history of depressive symptoms were examined.

Results

Lifetime prevalence estimates of 26.5% and 12.9% were reported by patients and rheumatologists, respectively. The 12-month prevalence rates reported by CORRONA patients and rheumatologists were 11.7% and 1.0%, respectively. The annualised IR from the self-reported depressive symptom measure was approximately 7.8 per 100 patient-years, compared to 0.4 per 100 patient-years reported by their rheumatologists. Increased disease activity at study entry was associated with a higher probability of reporting a history of depressive symptoms.

Conclusion

RA patients have a high likelihood of experiencing symptoms of depression, while treating rheumatologists under-report them and disease estimates based on their reports were much lower when compared to healthy individuals. Thus, estimates of prevalence and the impact of these symptoms need to be interpreted based on the source of the diagnosis. Collectively, the findings of this study suggest that depressive symptoms are an important comorbidity that practicing rheumatologists should be aware of during clinical encounters.

Key words

rheumatoid arthritis, depression, epidemiology

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Introduction

Depression is common in patients with rheumatoid arthritis (RA), the most prevalent autoimmune inflammatory arthritis, affecting 1.29 million American adults 18 years or older (1, 2). Studies using diagnostic criteria have estimated the point prevalence of this comorbidity in RA patients to be between 10%–23% (3-6). Furthermore, a meta-analysis determined that symptoms of depression are more common in RA patients when compared to healthy controls, independent of sociodemographic characteristics (2). Comparatively, the 12-month prevalence in the adult American population is 6.6%, which is approximately half, or less, than the rate observed in the RA population (7).

The consequences of depressive symptoms in RA are varied and far reaching and may influence disease activity, treatment persistence, and clinical outcomes from therapy (8-12). Research has shown that symptoms of depression are temporally associated with future increases in pain and increased moderating effects on disease activity (8, 9). The presence of depression may also impact disease modifying anti-rheumatic drug treatment and could result in an increased risk for medication discontinuation and inadequate response (10-12). Moreover, it exacerbates the impact of RA on overall health and is associated with higher mortality, an increased risk for myocardial infarction, greater work disability, and elevated healthcare expenditures (13-16). Despite the potential consequences, researchers suggest that as a comorbidity it is often not recognised nor prioritised by rheumatologists during routine rheumatology care (17, 18).

Given the high frequency and its association with unfavourable RA outcomes, this is an important condition that practicing rheumatologists should be aware of in their patients. Health care management for RA is chronic, and patients often have more visits with their rheumatologists as compared to their primary care provider (PCP), and some patients forego having a PCP given the close relationship with their arthritis care provider (19). However, a study examining communication about depressive symptoms revealed that among RA patients classified with a moderate to severe expression, only 19% discussed the issue during visits with their rheumatologists, and in every instance, the conversation was initiated by the patient (20). In contrast, research has demonstrated that in the primary care setting, where depression symptoms are discussed during 25% of visits, patients begin the dialogue approximately 55% of the time (21).

No research has assessed symptoms of depression using patient and physician depression measures reported separately from patients and rheumatologists in a large RA registry population. The study objectives were to:

1. calculate depressive symptom rates separately using patient- and rheumatologist-reported depression measures, and
2. examine the cross-sectional association of RA disease activity with a history of depression symptoms, using a national RA registry. We postulated there would be a high burden of prevalent and incident reports of depressive symptoms and that greater RA disease severity would be associated with a higher likelihood of prior manifestation.

Methods

Data source

The data for this study were an existing longitudinal cohort, the Consortium of Rheumatology Researchers of North America (CORRONA) registry. The operation and funding mechanisms for the CORRONA registry have been published previously (22). Patients enrolled in the CORRONA registry are recruited during routine clinical visits from academic and community rheumatology practices and are followed as often as every three months. Data collection began in 2001 and as of August 2012, data had been collected on >33,000 RA patients from 150 academic and community rheumatology practices across the United States (US). Data are gathered from patients and clinicians using standardised enrolment and follow-up survey forms and capture information on demographics, disease activity, disease severity, medication use, adverse events, and comorbidity. CORRONA data collected up until August 2012

were used for the present analyses. Patients are approved for enrolment into the CORRONA registry through the Institutional Review Boards (IRB) of institutions or a central IRB for academic and community rheumatology practices, respectively.

Study population

RA patients (n=15,604) enrolled between July 1, 2008 and August 13, 2012, the time period where both patient-reported and rheumatologist-reported depression measures were available, were used for the analyses (Supplementary Fig. 1). This sample was restricted to those with no missing self-reported and rheumatologist-reported depression data at study entry (n=14,755), and it was used to evaluate the lifetime prevalence of depression symptoms. To examine the 12-month prevalence, participants (n=14,594) with reported depression data at the time of enrolment but no symptom onset information (n=161) were restricted. For incident reports of depressive symptoms, patients were limited to a sample (n=7,555) where those with a history of prior manifestation at enrolment (n=4,190) and no follow-up visits (n=3,010) were excluded. The cross-sectional analysis was conducted using the primary analytic cohort (n=14,755), among patients with no missing data on possible confounders (n=11,506), and the primary factor of missing information was antidepressant medication use (n=1,519).

Measures

The depression symptom measures were single-item assessments. CORRONA data collection forms obtain information on ever having depression symptoms at enrolment, the time of onset, and the presence of depressive symptoms at follow-up visits. Patient enrolment surveys instruct participants to, "Please fill a 'NO' or 'YES' circle for each of the following conditions you have EVER had," including "Depression (Feeling Blue)." This measure incorporates a component for the time of comorbidity onset where patients can indicate "YES" in the context of categorical indicators (*e.g.* "YES 1–5 years ago"). Rheumatologist enrolment forms collect comorbidity data, including the time of onset, and rheumatologists are instructed to do the following: "If the patient has or has had any of the following," which contains an item for "Depression" and the "MM/YY" time of onset. Follow-up forms ask participants to indicate any "Medical condition or symptom you have had SINCE YOU LAST FILLED OUT THIS FORM," and has an item for "Depression (Feeling Blue)". The rheumatologist follow-up surveys collect data on all new comorbities and have the same instructions and items as the enrolment forms.

Depression as described in this study does not imply major depressive disorder (MDD) as diagnosed using DSM criteria. However, self-reported depressive symptoms, including questions about being "depressed," are what are commonly used to assess the condition during routine clinical care (23). Single-item patient-reported depression symptom measures have been used in prior research in a RA registry population and have demonstrated adequate reliability and convergent validity, and meta-analysis data suggests a high level of sensitivity but low specificity (24). Our process reflects the current American health care system, where patients are often the source of medical information and responsible for communicating between different providers when electronic medical records are not available. PCPs do not regularly send clinical updates to specialists, and research has shown that general practitioners have a greater accuracy in reporting medical problems when compared to specialists (25). Rheumatologists must ask patients about diagnoses and care they received from other physicians and during survey data collection participating CORRONA rheumatologists must discuss changes in their patient's health status to obtain past and present comorbidity information. Given they have to acquire such data directly from patients the rheumatologist-reported measure is a reflection of whether they communicate with them about depression at clinical visits.

Disease activity was assessed using composite indices, joint counts, global assessments, pain, and functional status. The clinical disease activity index (CDAI) is a summary score of the tender joint count based on 28 counts (TJC), swollen joint count based on 28 counts (SJC), patient global assessment of disease activity (PGA; visual analogue scale (VAS) 0–10 cm), and physician global assessment of disease activity (EGA; VAS 0–10 cm) (26). The 28 joint count disease activity score (DAS28) is calculated from the TJC, SJC, PGA, and the erythrocyte sedimentation rate (ESR) using a formula (27). The other measures that were used included the core component assessments previously described: TJC, SJC, PGA, and EGA; and patient pain (VAS 0–10 cm) and the health assessment questionnaire score (HAQ), converted from the modified HAQ (mHAQ) values (28).

Self-reported demographic variables included gender, age, race/ethnicity, education, marital status, employment, and health insurance. Race/ethnicity was reported as one the following: White, Black, Asian, Other, or Hispanic. Patients' age at enrolment was categorised: 18–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75–84, and 85+. Education level was captured as one of four categories: primary, high school, college/university, and don't remember. Marital status was coded into 4 groups: single, married/partnered, widowed, and divorced/separated; and employment was characterised using the following categories: full time, part time, unemployed, student, disabled, and retired. Lastly, health insurance was organised into four mutually exclusive groups groups: none, Medicaid, Medicare, and private.

Other covariates were smoking, alcohol use, exercise habits, body mass index (BMI), antidepressant use, comorbidity, and disease duration. Smoking and alcohol were binary measures (yes *vs.* no), and exercise was one of five categories: not at all, 1–2 times per week, 3–4 times per week, 5–6 times per week, and daily. Comorbidity was measured as a composite index (0-9) based on reports of past or present conditions from either the patient or physician that included myocardial infarction, stroke, hypertension, other cardiovascular disorders, diabetes mellitus, pulmonary disease, cancer, peptic ulcer, other gas-

trointestinal disorders, and fractures (29). Antidepressant use was captured as the current utilisation of any medications reported by patients.

Statistical analysis

The analyses were conducted in the common sample restricted to where both depression measures were available. Lifetime prevalence was defined as a history of symptoms of depression at study enrolment; 12-month prevalence was operationalised as having both a history of symptoms at enrolment and a reported onset occurring in the last year; and incident as the first longitudinal report in patients with no prior expression. Associations with the previously described covariates, except disease activity, were examined separately for the two different baseline depression measures, using *t*-tests, chi-square tests, and Wilcoxon rank sum tests, between those reporting and not reporting a history of depressive symptoms. Prevalence estimates and annualised incidence rates (IRs) were calculated overall by gender, race, ethnicity, and baseline age grouping.

Standardised lifetime prevalence estimates were calculated two ways: (1) standardising CORRONA rates to gender and age distributions given in publications; and (2) standardising estimates obtained from manuscripts to the CORRONA RA population. This was done to illustrate the impact of patient demographics on depression symptom estimates. Demographic data in manuscripts was given by gender and by age groups, and thus the calculations assumed that age distributions were equal between genders. CORRONA estimates were standardised to 2000 U.S. census data used in Kessler *et al*. (7) and the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) population distribution provided in Grant *et al*. (30). To apply estimates from NESARC data in Hasin *et al*. (31) given by age and by gender, age specific depression rates within each gender had to be generated. The NESARC estimates given by age and by gender were assumed to have a constant ratio of the rates by age group within each gender. Using the known NESARC population distribution, age specific prevalence rates were calculated within each gender, and then standardised to the CORRONA RA population.

Mixed-effects logistic regression was used to examine the cross-sectional association of RA disease activity with prior depressive symptoms at study entry. There were two outcomes: a history of (1) patient-reported and (2) rheumatologist-reported symptoms of depression. CORRONA data is structured such that patients are nested within rheumatologists, and rheumatologists are clustered in clinical sites. Patient outcome models were clustered by site as standard error estimates were similar to the fully nested model, and there was a low within-rheumatologist correlation after accounting for within site correlations. Rheumatologist outcome models were clustered by rheumatologists because the measure was reported by the treating medical specialist, and standard error estimates were comparable to the fully nested models. Predictor variables included the previously described RA disease activity measures, and to compare each of the different disease activity measures across multivariable models, they were coded as categorical quintiles. Unadjusted associations were evaluated and models adjusting for possible confounders that were selected a priori.

Results

Patient characteristics

The study population comprised 14,755 RA patients, and their characteristics at enrolment by depression history and measurement source are shown in Table I. Participants were predominantly middle-aged females, and there were significant differences for all baseline covariates by reported depression symptom history for every variable except education. The associations of patient attributes with prior depressive symptoms were similar for the two depression measures. Those with a prior manifestation at study entry were more likely to be female, younger, divorced or separated, and not have full time employment. Also, in patients with a history of symptoms, there was a higher frequency of smoking, lower levels of exercise, and increased disease duration, BMI, comorbidity, and antidepressant use.

Patient-reported prevalence

Of the 14,755 CORRONA RA patients, 26.5% reported a history of depression symptoms, which was most common in females, those white or reporting a race of other, and the middle aged, while lower among males, Asians, the young, and elderly (Table II). Restricted to cases of depression within 1-year of onset, the 12-month prevalence was 11.7%. However, the observed patterns by patient demographics were similar between the self-reported lifetime and 12-month prevalence of depressive symptoms, and the previously described trends persisted among those with a more recent onset. The standardised CORRONA patient-reported lifetime prevalence rates were approximately 22% (Table III). A reciprocal effect was observed when standardising NESARC rates to the CORRONA RA population. The estimate increased from 13.2% to 15.0%.

Rheumatologist-reported prevalence

The rheumatologist-reported lifetime and 12-month prevalence of depression symptoms was 12.9% and 1.0%, respectively (Table IV). Prior depressive symptoms reported by rheumatologists was more common in females, those white or reporting a race of other, and the middle-aged, resembling the demographic patterns regarding patient-reported prevalence. The rheumatologist-reported 12-month prevalence estimates exhibited the same trends concerning patient demographics as the rheumatologist-reported lifetime prevalence rates. The primary difference was the markedly smaller proportion of events with an onset occurring in the past year. After standardisation, the rheumatologist-reported lifetime prevalence of depression symptoms was 10.5% (*data not shown*), a decrease from the original estimate (12.9%).

Incident reports

The annualised depressive symptom IRs reported by CORRONA RA patients and rheumatologists were 7.8 per

Table I. General descriptive data in CORRONA RA patients for the primary analytic cohort by depression status concerning each of the two depression measures.

Variable	Measurement Source: Patient-Reported Depression Yes (n=3,903)	Patient-Reported Depression No (n=10,852)	*p*	Clinician-Reported Depression Yes (n=1,906)	Clinician-Reported Depression No (n=12,849)	*p*
Female	3,313 (85.01%)	8,012 (73.88%)	<0.001	1,634 (85.73%)	9,691 (75.50%)	<0.001
Race/Ethnicity						
White	3,274 (84.34%)	8,983 (83.03%)	<0.001	1,687 (88.60%)	10,570 (82.60%)	<0.001
Hispanic	234 (6.03%)	635 (5.87%)		93 (4.88%)	776 (6.06%)	
Black	275 (7.08%)	873 (8.07%)		93 (4.88%)	1,055 (8.24%)	
Asian	36 (0.93%)	214 (2.02%)		4 (0.21%)	246 (1.92%)	
Other	63 (1.62%)	114 (1.05%)		27 (1.42%)	150 (1.17%)	
Age[1] (yrs)	56.9 ± 12.8	58.1 ± 14.0	<0.001	57.1 ± 12.7	57.9 ± 13.8	0.03
Education						
Primary	87 (2.30%)	283 (2.69%)	0.38	52 (2.83%)	318 (2.55%)	0.26
High School	1,518 (40.17%)	4,320 (41.07%)		771 (41.92%)	5,067 (40.67%)	
College/University	2,153 (56.97%)	5,862 (55.73%)		1,011 (54.98%)	7,004 (56.22%)	
Don't Remember	21 (0.56%)	54 (0.50%)		5 (0.27%)	69 (0.55%)	
Insurance						
None	93 (2.40%)	259 (2.40%)	<0.001	47 (2.48%)	305 (2.39%)	<0.001
Medicaid	185 (4.78%)	249 (2.31%)		82 (4.33%)	352 (2.76%)	
Medicare	804 (20.78%)	2,074 (19.24%)		429 (22.64%)	2,449 (19.20%)	
Private	2,788 (72.04%)	8,200 (76.05%)		1,337 (70.55%)	9,651 (75.65%)	
Marital status						
Single	446 (11.70%)	1,290 (12.20%)	<0.001	203 (10.88%)	1,533 (12.24%)	<0.001
Married/Partnered	2,345 (61.52%)	7,188 (67.96%)		1,157 (62.0%)	8,376 (66.88%)	
Widowed	361 (9.47%)	971 (9.18%)		194 (10.40%)	1,138 (9.09%)	
Divorced/Separated	660 (17.31%)	1,128 (10.66%)		312 (16.72%)	1,476 (11.79%)	
Employment						
Full Time	1,230 (31.59%)	4,529 (41.80%)	<0.001	588 (30.88%)	5,171 (40.32%)	<0.001
Part Time	325 (8.35%)	945 (8.72%)		141 (7.41%)	1,129 (8.80%)	
Unemployed	522 (13.41%)	1,088 (10.04%)		255 (13.39%)	1,355 (10.57%)	
Student	29 (0.74%)	109 (1.01%)		12 (0.63%)	126 (0.98%)	
Disabled	806 (20.70%)	837 (7.73%)		384 (20.17%)	1,259 (9.82%)	
Retired	982 (25.22%)	3,326 (30.70%)		524 (27.52%)	3,784 (29.51%)	
Disease duration[1] (yrs)	8.4 ± 9.6	8.2 ± 9.4	0.22	8.8 ± 9.7	8.2 ± 9.4	0.02
Alcohol Use	1,829 (47.73%)	5,195 (48.71%)	0.30	864 (46.01%)	6,160 (48.82%)	0.02
Smoking	704 (18.40%)	1,493 (13.99%)	<0.001	352 (18.78%)	1,845 (14.61%)	<0.001
Exercise						
None	1,427 (37.73%)	3,409 (32.33%)	<0.001	745 (39.86%)	4,101 (32.87%)	<0.001
1-2 times/week	1,209 (31.97%)	3,073 (29.14%)		606 (32.42%)	3,679 (29.49%)	
3-4 times/week	688 (18.19%)	2,244 (21.28%)		300 (16.20%)	2,632 (21.10%)	
5-6 times/week	168 (4.44%)	699 (6.63%)		79 (4.27%)	888 (6.32%)	
Daily	290 (7.67%)	1,121 (10.63%)		135 (7.29%)	1,276 (10.23%)	
BMI (kg/m^2)	30.8 ± 7.5	28.9 ± 6.7	<0.001	30.9 ± 7.4	29.1 ± 6.9	<0.001
Comorbidity[2]	1 (0-2)	1 (0-2)	<0.001	1 (1-2)	1 (0-2)	<0.001
Antidepressant sse	2,153 (59.96%)	871 (9.18%)	<0.001	1,192 (66.52%)	1,832 (16.24%)	<0.001

[1]Continuous value given as the mean value and standard deviation; [2]Contiunous value given as the median and IQR.

100 patient-years and 0.4 per 100 patient-years, respectively (Table V). IR trends were similar across gender, race/ethnicity, and age groups by depression measurement modality, but in some subgroups, there was a lack of rheumatologist-reported events. Specifically, there were no rheumatologist-reported events in the lowest and high age stratums and patients identifying as Asian or Other. Incident reports of symptoms were more common in females, Hispanics and Whites, but did not display any particular patterns by baseline age grouping. The most prominent attribute was the difference in IRs between the two measurements sources, where the RA patients reported a much larger number of incident events when compared to their treating rheumatologists.

Cross-sectional associations

Cross-sectional associations of disease activity with a history of patient-reported symptoms of depression are displayed in Table VI, and results for the rheumatologist-reported outcome are in shown in Supplementary Table I. In unadjusted models, every measure of disease activity was positively associated with prior depressive symptoms for both outcome measures. Higher disease activity at study entry was associated with an increased likelihood of reporting past symptoms of depression, and unadjusted effect sizes were compara-

Table II. Patient-reported lifetime and twelve-month depression prevalence estimates by gender, race/ethnicity, and age group.

	Patient-Reported Lifetime Prevalence[¶]				Patient-Reported 12-Month Prevalence[‡]			
Group	n	Events	Prevalence	95% CI	n	Events	Prevalence	95% CI
Overall	14,755	3,903	26.45%	[25.74-27.16]	14,594	1,714	11.74%	[11.22-12.27]
Male	3,417	584	17.09%	[15.83-18.35]	3,393	253	7.46%	[6.57-8.34]
Female	11,325	3,313	29.25%	[28.42-30.09]	11,193	1,461	13.05%	[12.43-13.68]
White	12,257	3,274	26.71%	[25.93-27.50]	12,130	1,449	11.95%	[11.37-12.52]
Hispanic	869	234	26.93%	[23.98-29.88]	862	99	11.48%	[9.36-13.62]
Black	1,148	275	23.95%	[21.49-26.43]	1,133	115	10.15%	[8.39-11.91]
Asian	250	36	14.40%	[10.04-18.76]	247	14	5.67%	[2.78-8.56]
Other	177	63	35.59%	[28.52-42.68]	174	26	14.94%	[9.63-20.26]
18-24	153	25	16.34%	[10.46-22.18]	142	8	5.63%	[1.83-9.44]
25-34	698	174	24.93%	[21.72-28.14]	675	74	10.96%	[8.60-13.32]
35-44	1,630	452	27.73%	[25.56-29.90]	1,616	195	12.07%	[10.48-13.66]
45-54	3,243	929	28.65%	[27.09-30.20]	3,217	412	12.81%	[11.65-13.96]
55-64	4,227	1,276	30.19%	[28.80-31.57]	4,192	558	13.31%	[12.29-14.40]
65-74	3,209	739	23.03%	[21.57-24.49]	3,175	348	10.96%	[9.87-12.05]
75-74	1,301	246	18.91%	[16.78-21.04]	1,290	94	7.29%	[5.87-8.71]
85+	272	54	19.85%	[15.10-24.60]	270	23	8.52%	[5.18-11.86]

[¶]Restricted to patients enrolled after July of 2008, among those with no missing data for patient-reported and clinician-reported depression prevalence at baseline.
[‡]Restricted to patients enrolled after July of 2008, among those with no missing data for patient-reported and clinician-reported depression prevalence and the associated time of onset at baseline.

Table III. Lifetime depression prevalence rates standardised by gender and by age.

Paper	Publication Population	Standard Population	Crude Prevalence	Standardised Prevalence	Comparator Prevalence
		Standardised CORRONA Lifetime Depression Prevalence			
Kessler *et al*. 2003	National Comorbidity Survey	2000 U.S. Census Data	• 26.29%	21.53% [20.30-22.76]	[†] 16.2% [15.1-17.3]
Grant *et al*. 2004 & Hasin *et al*. 2005	National Epidemiologic Survey on Alcohol and Related Conditions	NESARC Participants	• 26.29%	21.63% [20.42-22.84]	[¥] 13.2% [12.6-13.8]
		Standardised NESARC Lifetime Depression Prevalence			
Grant *et al*. 2004 & Hasin *et al*. 2005	National Epidemiologic Survey on Alcohol and Related Conditions	CORRONA RA Patients	□13.23%	15.04% [14.58-15.51]	[‡] 26.5% [25.7-27.2]

•Crude lifetime prevalence is from the CORRONA RA population.
□Crude lifetime prevalence is from the NESARC population.
[†]Comparator lifetime prevalence is from Kessler *et al*. using the NCS.
[¥]Comparator lifetime prevalence is from Hasin *et al*. using the NESARC.
[‡]Comparator lifetime prevalence is from the CORRONA RA population.

ble between the two outcome measures. Of the predictors associated with a history of manifestation, the strongest in magnitude were the PGA, patient pain, and HAQ. Adjustment for possible confounders attenuated the associations, and this decrease in risk was greater when using the rheumatologist-reported outcome measure. For the patient-reported outcome, the DAS28 and SJC lost statistical significance, compared to the DAS28, SJC, and EGA, regarding the rheumatologist-reported outcome. Sensitivity analyses incorporating concomitant treatment factors at study entry into multivariable models yielded similar findings.

Discussion

In this RA registry, there were high patient-reported levels of prevalent depressive symptoms, greater than the general population (7, 31). Conversely, the rheumatologist-reported prevalence estimates were consistently equal to, or lower than, national estimates (7, 31). CORRONA patient-reported depressive symtpom IRs were higher compared to estimates from the National Databank for Rheumatic Diseases (NDB) and rates for healthy individuals from studies using community based samples, while those reported from their treating rheumatologists were lower (29, 32). The cross-sectional results parallel other studies demonstrating that disease activity is associated with symptoms of depression, yet the adjusted effect sizes and number of significant associations was greater for the patient-reported outcome (33, 34). The findings suggest a high prevalence of depressive symptoms among CORRONA RA patients, under-reporting of their presence by rheumatologists, and that increased disease activity is associated with its past manifestation.

If the patient-reported estimates were extrapolated, they would imply that one-fourth of RA patients have prior symptoms of depression and that 11% of the time they occurred within the

Table IV. Rheumatologist-reported lifetime and twelve-month depression prevalence estimates by gender, race/ethnicity, and age group.

	[¶]Rheumatologist-Reported Lifetime Prevalence				[‡]Rheumatologist-Reported 12-Month Prevalence			
Group	n	Events	Prevalence	95% CI	n	Events	Prevalence	95% CI
Overall	14,755	1,906	12.92%	[12.38-13.46]	14,594	145	0.99%	[0.83-1.16]
Male	3,417	272	7.96%	[7.05-8.87]	3,393	30	0.88%	[0.57-1.20]
Female	11,325	1,634	14.43%	[13.78-15.08]	11,193	115	1.03%	[0.84-1.21]
White	12,257	1,687	13.76%	[13.15-14.37]	12,130	127	1.05%	[0.87-1.23]
Hispanic	869	93	10.70%	[8.65-12.76]	862	7	0.81%	[0.21-1.41]
Black	1,148	93	8.10%	[6.52-9.68]	1,133	9	0.79%	[0.28-1.31]
Asian	250	4	1.60%	[0.04-3.16]	247	0	0.00%	–
Other	177	27	15.25%	[9.94-20.57]	174	2	1.15%	[-0.44-2.74]
18-24	153	14	9.15%	[4.57-13.73]	142	1	0.70%	[-0.68-2.09]
25-34	698	89	12.75%	[10.27-15.23]	675	9	1.33%	[0.47-2.20]
35-44	1,630	212	13.01%	[11.37-14.64]	1,616	24	1.49%	[0.90-2.08]
45-54	3,243	417	12.86%	[11.71-14.01]	3,217	37	1.15%	[0.78-1.52]
55-64	4,227	649	15.35%	[14.27-16.44]	4,192	38	0.91%	[0.62-1.20]
65-74	3,209	382	11.90%	[10.78-13.03]	3,175	26	0.82%	[0.51-1.13]
75-74	1,301	118	9.07%	[7.51-10.63]	1,290	9	0.70%	[0.24-1.15]
85+	272	25	9.19%	[5.75-12.63]	270	1	0.37%	[-0.36-1.10]

[¶]Restricted to patients enrolled after July of 2008, among those with no missing data for patient-reported and clinician-reported depression prevalence at baseline.
[‡]Restricted to patients enrolled after July of 2008, among those with no missing data for patient-reported and clinician-reported depression prevalence and the associated time of onset at baseline.

Table V. Gender, race, and age specific annualised incidence rates by depression measurement modality.

	[¶]Patient-Reported Depression				[¶]Clinician-Reported Depression			
	n	Events	Person Time (years)	[¥]Incidence Rate	n	Events	Person Time (years)	[¥]Incidence Rate
Overall	7,555	914	11,764	7.77 [7.28-8.29]	7,555	46	12,572	0.37 [0.27-0.49]
Male	1,972	195	3,114	6.26 [5.44-7.21]	1,972	12	3,287	0.37 [0.21-0.64]
Female	5,581	719	8,646	8.32 [7.73-8.95]	5,581	34	9,281	0.37 [0.26-0.51]
White	6,296	751	9,913	7.58 [7.05-8.14]	6,296	41	10,586	0.39 [0.28-0.53]
Hispanic	393	56	508	11.03 [8.49-14.33]	393	3	550	0.55 [0.18-1.69]
Black	626	87	937	9.28 [7.52-11.45]	626	2	1,009	0.20 [0.05-0.79]
Asian	147	11	261	4.21 [2.33-7.60]	147	0	274	–
Other	74	8	130	6.15 [3.08-12.30]	74	0	138	–
18-24	89	13	118	11.02 [6.40-18.98]	89	0	127	–
25-34	345	44	498	8.83 [6.58-11.87]	345	2	541	0.37 [0.09-1.48]
35-44	808	96	1,268	7.57 [6.20-9.25]	808	12	1,348	0.89 [0.51-1.57]
45-54	1,678	249	2,626	9.48 [8.38-10.74]	1,678	10	2,861	0.35 [0.19-0.65]
55-64	2,075	260	3,291	7.90 [6.99-8.92]	2,075	10	3,533	0.28 [0.15-0.53]
65-74	1,710	162	2,694	6.01 [5.16-7.01]	1,710	10	2,834	0.35 [0.19-0.66]
75-74	706	76	1,072	7.09 [5.67-8.88]	706	2	1,124	0.18 [0.05-0.71]
85+	138	13	189	6.86 [3.98-11.82]	138	0	195	-

[¶]Restricted to patients enrolled after July of 2008, among those with no missing data and reports of prevalent depression for the patient and clinician depression measures at baseline.
[¥]Incidence rates (IR) are reported per 100 patient-years of observation.

past year. The age and gender standardised CORRONA lifetime prevalence estimate of 22% is substantially higher than comparator rates from U.S. general population (13%-16%) (7,31). Moreover, the 12-month prevalence (11.1%) is on the lower end of the spectrum of estimates for the point prevalence of depression in RA patients (10%-23%) (3-6), yet still higher than the general population (6.6%) (7). These data suggest a high prevalence of depressive symptoms among CORRONA RA patients, and given that prior research has consistently demonstrated that patients have a strong ability to recall prior comorbidities when validated against chart abstractions, external raters, and laboratory results, any measurement bias is likely to be minimal (35-37).

The rheumatologist-reported lifetime prevalence indicates a similar likelihood of ever having symptoms of depression when compared to the general population (12.8% vs. 13%-16%) (7, 31), but adjustment for age and gender would suggest a lesser risk. The 12-month prevalence rate (1.0%) is lower than the national estimates (6.6%) and results from cross sectional studies in other RA samples (10%-23%) (3-7). The point prevalence of depression in RA is ≥10%, and therefore, it is unlikely that the risk of depressive symptoms among RA patients is lower than healthy individuals (3-7).

Table VI. Unadjusted and adjusted associations of RA disease activity with the patient-reported lifetime prevalence of depression in the CORRONA registry.

			†Unadjusted			†Adjusted		
Variable		n	OR	95% CI	*p*	OR	95% CI	*p*
CDAI	Quintile 1	2,353	–	-	<0.001	–	–	<0.001
	Quintile 2	2,189	1.59	[1.37-1.84]		1.36	[1.14-1.61]	
	Quintile 3	2,273	1.81	[1.57-2.10]		1.40	[1.18-1.66]	
	Quintile 4	2,303	2.21	[1.92-2.56]		1.66	[1.39-1.97]	
	Quintile 5	2,232	2.64	[2.28-3.06]		1.67	[1.39-1.99]	
DAS28	Quintile 1	1,175	–	–	<0.001	–	–	0.31
	Quintile 2	1,175	1.32	[1.08-1.60]		1.09	[0.86-1.38]	
	Quintile 3	1,175	1.56	[1.29-1.90]		1.22	[0.97-1.55]	
	Quintile 4	1,174	1.87	[1.54-2.27]		1.21	[0.96-1.53]	
	Quintile 5	1,174	1.96	[1.61-2.38]		1.26	[0.99-1.61]	
TJC	Quintile 1	3,961	–	-	<0.001	–	–	<0.001
	Quintile 2	1,179	1.14	[0.97-1.33]		1.11	[0.92-1.34]	
	Quintile 3	1,917	1.41	[1.24-1.61]		1.32	[1.13-1.54]	
	Quintile 4	2,340	1.50	[1.32-1.69]		1.22	[1.05-1.42]	
	Quintile 5	2,094	2.02	[1.78-2.28]		1.45	[1.24-1.68]	
SJC	Quintile 1	4,085	–	–	0.002			0.40
	Quintile 2	1,110	1.08	[0.93-1.26]		1.16	[0.96-1.39]	
	Quintile 3	1,916	1.03	[0.90-1.17]		1.07	[0.91-1.24]	
	Quintile 4	2,169	1.23	[1.09-1.39]		1.13	[0.97-1.31]	
	Quintile 5	2,210	1.22	[1.08-1.38]		1.11	[0.95-1.28]	
PGA	Quintile 1	2,746	–	–	<0.001	–	–	<0.001
	Quintile 2	1,843	1.23	[1.05-1.43]		1.18	[0.98-1.41]	
	Quintile 3	2,285	2.07	[1.80-2.38]		1.68	[1.43-1.98]	
	Quintile 4	2,594	2.50	[2.19-2.85]		1.75	[1.49-2.06]	
	Quintile 5	1,966	3.33	[2.89-3.83]		2.03	[1.71-2.41]	
EGA	Quintile 1	2,736	–	–	<0.001	–	–	<0.001
	Quintile 2	2,634	1.26	[1.10-1.44]		1.10	[0.94-1.28]	
	Quintile 3	1,855	1.44	[1.25-1.66]		1.14	[0.96-1.36]	
	Quintile 4	1,932	1.47	[1.27-1.69]		1.23	[1.04-1.45]	
	Quintile 5	2,266	1.95	1.71-2.24]		1.44	[1.22-1.70]	
Patient-Pain VAS	Quintile 1	2,438	–	–	<0.001	–	–	<0.001
	Quintile 2	2,397	1.31	[1.13-1.52]		1.14	[0.96-1.36]	
	Quintile 3	2,153	2.04	[1.77-2.36]		1.53	[1.29-1.81]	
	Quintile 4	2,558	2.53	[2.21-2.90]		1.67	[1.42-1.97]	
	Quintile 5	1,884	3.11	[2.69-3.61		1.83	[1.53-2.18]	
HAQ	Quintile 1	2,306	–	–	<0.001	–	–	<0.001
	Quintile 2	2,210	1.38	[1.17-1.61]		1.04	[0.85-1.27]	
	Quintile 3	2,256	2.18	[1.85-2.53]		1.41	[1.18-1.69]	
	Quintile 4	2,261	2.82	[2.44-3.27]		1.74	[1.45-2.09]	
	Quintile 5	2,253	4.07	[3.52-4.71]		2.05	[1.69-2.48]	

†Indicates mixed effects models were clustered by data collection site.
Confounders: age, gender, race, ethnicity, marital status, education, employment, health insurance, disease duration, BMI, composite comorbidity, smoking, alcohol consumption, exercise, and anti-depressant use.

The rheumatologist-reported prevalence estimates are similar to Medical Outcomes Study data showing that among primary care patients with current symptomology indicative of depression, the condition goes unrecognised approximately 50% of the time by general practitioners during routine clinical visits (38).

The self-reported IR of 7.7 per 100 patient-years was much higher than the rheumatologist-reported rate of 0.4 per 100 patient-years. The patient rates are generally higher than estimates for the incidence of depression in the general population, while the rheumatologist-reported rate is less than one-fourth of the lowest observed rate in normal individuals (1.8-7.5 per 100 patient-years) (32). The rate reported by rheumatologists seems improbably low and is discouraging because current National Institute for Health and Clinical Excellence (NICE) guidelines recommend that physicians be aware of symptoms of depression in patients with chronic physical disease (39). The rheumatologist-reported rate is questionable considering that RA patients have chronic arthritis symptoms that are associated with the presence and severity of depressive symptoms (33, 34, 40-42), and thus are predisposed for their manifestation, evidenced by previous studies that have shown a high prevalence (16.8%) in the RA population that is greater than normal individuals (6.6%) (7, 43).

Prior symptoms of depression were associated with every RA disease activity measure, but these predictors had a stronger correlation with the patient-reported outcome. Many studies have examined cross-sectional associations between prevalent depressive symptoms and RA disease activity, and pain and functional status have been consistently linked to their presence (3, 33, 34, 44). These variables were amongst the most strongly associated with past depressive symptoms; however, the CDAI, TJC, and PGA were also associated with the outcomes. The difference in the magnitude and number of adjusted significant associations between the outcomes parallels the descriptive data and could explain the lower adjusted effect sizes for the rheumatologist-reported outcome. Given that disease activity displayed the hypothesised associations that are similar to data from prior cross-sectional studies (33, 34, 40-42, 44), but also corresponded to the observed differences in the CORRONA population rates, these results further confirm the validity of the patient-reported measure of depressive symptoms to identify this comorbidity.

This study also has some limitations. The single-item depressive symptom measures are not indicative of depression as diagnosed by DSM criteria, and neither the frequency nor severity of the symptoms was assessed. Also, there were slight differences between the patient and rheumatologist depression metrics, which may have influenced the results. The patient-reported measure is more an assessment of symptoms of depression, which repre-

sents the core expression of the disorder, rather than a measure of clinical depression. This could have resulted in a degree of overestimation regarding the patient-reported rates, but when the results of this study were contrasted to prior research, the presence of such bias seemed very minimal. Moreover, feeling "depressed" is a critical symptom of depression and is what is typically used in routine clinical practice to identify patients with this comorbidity (23).

There are several implications from this research. The data revealed high patient-reported depression symptom rates in a large registry sample, and conversely, rheumatologist-reported comorbidity rates that were much lower than what their patients indicated. Additionally, cross-sectional analyses demonstrated strong associations between multiple domains of disease activity and prior symptoms of depression that paralleled the descriptive results. Based on the known depression rates in RA patients and the general population, the rheumatologist-reported estimates are implausibly low and likely represent under-reporting. Current literature would suggest the cause is a lack of awareness about depression among rheumatologists (20), and studies have shown that medical specialists are not attentive to depressive disorders (23). This gap in clinical care needs to be addressed because depression in RA is associated with worse overall health, increased disease activity, decreased medication persistence, lower therapeutic response, and difficulties in medical management (13-16, 45, 46). Consequently, and in accordance with NICE guidance, rheumatologists need to regularly assess for the presence of affective symptoms in their patients to provide the best care possible and address any challenges due to depression (39). To better understand the epidemiology and severity of depressive symptomology in their RA patients, rheumatologists could regularly ask patients about the condition or utilise 1- or 2-item ultra-brief symptom measures, such as the Patient Health Questionnaire-2 item scale, which have high sensitivity and specificity and been validated in patients with chronic physical disease (47, 48).

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