Pain and other self-reported scores in patients with osteoarthritis indicate generally similar disease burden to patients with rheumatoid arthritis

J.R. Chua¹, K.A. Gibson²⁻⁴, T. Pincus¹

¹Department of Internal Medicine, Division of Rheumatology, Rush University Medical Center, Chicago, IL, USA. ²Department of Rheumatology, Liverpool Hospital, NSW; ³Ingham Research Institute, Liverpool, NSW, Australia; ⁴University of New South Wales, Kensington, Sydney, NSW, Australia. Jacquelin R. Chua, MD

Kathryn A. Gibson, MD, PhD Theodore Pincus, MD

Please address correspondence to: Dr Theodore Pincus, Division of Rheumatology, Rush University Medical Center, 1611 West Harrison Street, Suite 510, Chicago, IL 60612, USA. E-mail: tedpincus@gmail.com

Received and accepted on September 11, 2017.

Clin Exp Rheumatol 2017; 35 (Suppl. 107): S88-S93.

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Key words: rheumatoid arthritis (RA), osteoarthritis (OA), routine assessment of patient index data (RAPID3), multidimensional health assessment questionnaire (MDHAQ), patient-reported outcomes

Competing interests: T. Pincus is president of Medical History Services, LLC, which receives royalties and license fees for a copyright and trademark for MDHAQ and RAPID3. All revenue supports further development of quantitative questionnaire measurement for patients and doctors in clinical care. Dr Pincus is also a consultant for Abbie, Lilly and Pfizer. J.R. Chua and K.A. Gibson have declared no competing interests.

ABSTRACT

Objective. Osteoarthritis (OA) is regarded as a less severe form of arthritis than rheumatoid arthritis (RA) by health professionals and the general public, based largely on laboratory findings of autoantibodies and acute phase reactants. Relatively few studies have reported data from the patient's perspective to compare directly OA versus RA using the same self-report questionnaire measure. We aimed to summarise reports that compare OA versus RA patient pain scores and other indicators of disease burden according to the same self-report questionnaire.

Methods. A retrospective review identified 5 published reports at 8 rheumatology sites in 4 countries from 1989 to 2017 in which patients with OA versus RA completed the same patient selfreport questionnaire for pain and other variables. Most comparisons involved a health assessment questionnaire (HAQ) and derivative multidimensional HAQ (MDHAQ), which include physical function, pain visual analogue scale (VAS) and patient global assessment VAS. Other questionnaires were included in one or two reported studies.

Results. Mean or median pain VAS was in a similar range in OA versus RA, though somewhat higher in OA at 7 of 8 sites studied (included in 1989). Physical function and other scores also were in a similar range for RA versus OA. Evidence of higher scores for physical function in RA relative to OA in earlier than more recent studies was seen, although all studies indicated a clinically important disease burden in OA.

Conclusion. *OA* presents a severe disease burden to patients, which appears similar to RA. The findings suggest revision of current clinical and public policy views concerning OA.

Introduction

Health professionals and the public generally regard rheumatoid arthritis (RA) as more severe than osteoarthritis (OA) (1-3). Laboratory findings of autoantibodies such as rheumatoid factor and anti-cyclic citrullinated antibodies (ACPA), and elevated acute phase reactants such as erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are regarded as "differentiating RA from....OA, which is a far more prevalent "low-grade" inflammatory articular disease (4). From the standpoint of inflammatory markers, systemic symptoms, and radiographs, the impression of RA as a more severe process is accurate.

A somewhat different picture emerges in quantitative comparisons of OA versus RA from a patient perspective. Both OA and RA patients experience substantial pain, functional disability, and other indicators of a similar disease burden. However, different measurement tools usually are used to assess the two diseases, a health assessment questionnaire (HAQ) (5) in RA versus a Western Ontario McMaster (WOMAC) scale (6) in OA. Direct comparisons of OA versus RA are available only when the same measure is used, but only a few reports present comparisons of OA versus RA using the same patient questionnaire measure.

This review summarises the only 5 such reports known to the authors, 4 of which indicate higher scores in OA *versus* RA on a pain visual analogue scale (VAS) (indicating poorer clinical status), including one report published in 1989, although scores were in a similar range. Furthermore, scores on other scales to assess physical function and quality of life generally indicate similar scores in patients with OA *versus* RA. These observations appear at variance with current beliefs concerning OA and RA.

The data are not interpreted to ask or determine whether OA or RA may be "more severe" at a group or individual level. Considerable variation in disease burden is seen in individual patients with OA or RA (or any disease) from very mild to very severe. We emphasize that composite evidence indicates that the majority of patients with OA, at least among those seen by rheumatologists, experience a severe disease burden, in a similar range to patients with RA (and vice versa for some individual patients). OA is 20-40 times as prevalent as RA (7) and presents a great disease burden to society (8-10), for which increased basic and clinical research appears indicated.

MDHAQ to document the greater significance of formal education: 1989 report

A 1989 report from Nashville, TN, USA presented a comparison of scores on a modified HAQ (MHAQ) (11), an antecedent of the multidimensional HAQ (MDHAQ) (12, 13), in 602 patients with five rheumatic diseases, including 134 with RA, 216 with OA, 84 with fibromyalgia, 124 with systemic lupus ervthematosus (SLE), and 43 with systemic sclerosis (14). This study was conducted to compare the significance of age, duration of disease, and formal education level in clinical status measures in each disease, with the observation that formal education level was more explanatory of variation in almost all comparisons than age or duration of disease (14). Retrospective analyses of reported data allow comparisons of clinical status measures in patients with OA versus RA.

Mean pain VAS scores were 6.01 in OA compared to 5.16 in RA (and 6.35 in fibromyalgia) (Table I) (14). By contrast, scores for physical function to perform 8 activities of daily living (ADL), pain in activities of daily living (the same activities as in the physical function scale), and patient global assessment on a 4-point scale were 0.16–1.25 units higher in RA compared to OA patients (Table I) (14). Nonetheless, these scores indicated a substantial disease burden in patients with OA.

Rasch analyses of the Western Ontario McMaster (WOMAC) scale: 1999 report

An early study reported in 1999 from Wichita KS, USA was directed at Rasch analysis of the WOMAC scale scores, to analyse intervals on a scale between different scores (Table II) (15). In these analyses, the VAS pain scale was scored on a 0-3 scale, and mean scores were 1.3 in OA and 1.1 in RA. In this review, these scores are adjusted to a 0-10 scale (by multiplication by 3.3) to 3.63 for RA and 4.89 for OA, to compare to scores in other reports, recognising that these adjustments are somewhat less precise.

All other scores were higher in OA compared to RA. WOMAC scores for function (range 0–170) were 65 in OA patients *versus* 53 in RA patients, WOM-AC pain scores (0-50) were 18.6 in OA *versus*14.9 in RA, HAQ disability was identical at 3.30 in both groups, and patient global severity on 0-100 scale was 38.7 in OA and 35.8 in RA (Table II) (15). The WOMAC was designed for use in OA, although the pain VAS was not, and HAQ disability scores designed for RA. All scores were identical or similar in either diagnosis, though indicating somewhat poorer status in OA (15).

Minimal clinical important differences (MCID) measured on a numerical rating scale (NRS): 2004 report

A prospective cohort study was conducted in Ancona, Italy to determine the minimal clinically important difference (MCID) of changes in chronic musculoskeletal pain intensity on a numerical rating scale (NRS) (21). The NRS scale in this study assessed pain severity by asking the patient to draw a single mark on a horizontally oriented, graduated 10-cm line, bounded by the descriptors "no pain" at the far left and "worst possible pain" at the far right (21). This method of scoring an NRS is virtually identical to a VAS (21, 22).

The study included 290 patients with RA and 233 patients with OA of the knee, 86 patients with OA of the hip, and 133 with OA of the hand. Patients with OA were generally older and had longer disease duration than patients with RA.

Median NRS scores were 6.5 cm for RA, 5.5 cm for OA of the knee, 6 cm for OA of the hip, and 5 cm for OA of the hand (Table IV). The scores were numerically higher in RA than in OA but the confidence intervals were overlapping except in patients with hand OA (21).

Direct comparisons of scores on several questionnaires in patients with hand OA *versus* RA: 2009 report

A report from Oslo, Norway in 2009 appears the earliest study to analyse directly differences in clinical status in OA versus RA (16). The study presents two differences form other studies in this review. First, patients were selected for having OA of the hand, although 9% had OA of the hip and 59% had OA of the knee according to American College of Rheumatology (ACR) Criteria (16) (Table III). Second, all patients were aged 50-70, and the mean age was 61.6 for hand OA and 61.1 for RA (16). In all the other studies, OA patients were older, although adjustment for age was included in all.

Patients completed several self-report questionnaires, including the HAQ (5), MHAQ (17), Arthritis Impact Measurement Scale 2 (AIMS2) (18), the 36item Short Form Health Survey (SF-36) (19), self-efficacy scales (20), and a fatigue VAS (16). Pain VAS score was 38.6 in the OA patients and 36.4 in the RA patients (p=0.35). Other measures of pain on the AIMS2 and SF-36 were higher in OA, although only AIMS2 differences were statistically significant, adjusted for multiple comparisons (Table III) (16).

Measures of physical function including on the AIMS2, SF-36, HAQ, and MHAQ, as well as a fatigue VAS, and SF 36 generally indicated poorer status in patients with RA compared with OA (16), as in the 1989 study above (14). The RA patients had been seen at the early stage in the use of biological agents in 2000–2002, and may have received lesser benefit from treatment than seen at present. Furthermore, although 68% of the patients also had OA of the hip or knee, 32% had only OA of the hand, with likely less functional disability than patients who also had lower extremity

Severity of osteoarthritis / J.R. Chua et al.

Table I. Comparison of questionnaire scores in patients with rheumatoid arthritis (RA) and osteoarthritis (OA): Callahan *et al.* 1989 (14).

	RA	OA	<i>p</i> -value	Poorer scores
Number of patients	134	216		
MHAQ – Physical function [‡]	3.10	1.86	< 0.001	RA
MHAQ - Pain in activities of daily living	2.37	2.08	< 0.001	RA
MHAQ – VAS Pain	5.16	6.01	< 0.001	OA
MHAQ – Global estimate	2.59	2.43	0.008	RA
	2.55	2.45	0.000	IC/ Y

*Transformed to 0-10 to compare with MDHAQ scores.

Table II. Comparison of questionnaire scores in patients with rheumatoid arthritis (RA) and osteoarthritis (OA): Wolfe and Kong 1999 (15).

	RA	OA	<i>p</i> -value	Poorer scores
Number of patients	1013	655		
WOMAC Function (range 0-170) (SD)	53.0 (39.1)	65.1 (40.9)		OA
WOMAC Pain (range 0-50) (SD)	14.9 (11.4)	18.6 (11.8)		OA
HAQ Disability (range 0-3) (SD)	3.30 (0.75)	3.30 (0.70)		=
VAS Pain (range 0-3) (SD)	1.1 (0.76)	1.3 (0.79)		OA
Patient global severity (range 0-100) (SD)	35.8 (24.0)	38.7 (24.4)		OA

Table III Comparison of numerical rating scale scores in patients with rheumatoid arthritis (RA) and osteoarthritis (OA): Salaffi *et al.* 2004 (21).

Numerical Rating Scale score (cm)	RA	OA-knee	OA-hip	OA-hands
Number of patients	290	233	86	133
Mean (SD) (0-10) (SD)	6.4 (1.5)	5.8 (1.6)	6.0 (1.7)	5.1 (1.6)
Median (0-10) (95% conf. interval)	6.5 (6.1-6.7)	5.5 (5.6-6.1)	6.0 (5.7-6.3)	5.0 (4.7-5.4)

Table IV. Comparison of questionnaire scores in patients with rheumatoid arthritis (RA) and osteoarthritis (OA): Slatkowsky-Christensen 2009 (16).

	RA OA		<i>p</i> -value	Poorer	
				500105	
Number of patients	194	190			
AIMS2 Physical	2.38	1.74	< 0.001*	RA	
SF-36 Physical Scale [¥]	47.9	58.3	<0.001*	RA	
HAQ – Physical (0-3) [‡]	4.09	3.03	<0.001*	RA	
MHAQ – Physical (1-4) [‡]	2.13	1.59	0.002*	RA	
VAS Pain (0-100)	36.4	38.6	0.35	OA	
AIMS2 Pain (0-10)	4.83	5.52	0.006*	OA	
SF-36 Pain Scale [¥] (0-100)	43.7	40.4	0.11	OA	
VAS Fatigue (0-100)	50.4	44.2	0.04	RA	
SF-36 Vitality [¥] (0-100)	42.9	41.0	0.40	OA	
VAS Global (0-100)	39.4	40.6	0.63	OA	
SF-36 General [¥] (0-100)	46.2	52.8	0.005*	RA	

* Statistically significant level (<0.014 after adjustment for multiple testing by Sime's procedure).

^{*}Transformed to 0-10 to compare with MDHAQ scores

[¥] Higher score indicates better status, unlike other measures for which higher score indicates poorer status.

involvement. Nonetheless, the scores for patients with RA were within 25% of those with OA, suggesting a relatively similar disease burden in both diseases.

Comparisons of RA *versus* OA at 4 sites with MDHAQ at each visit in all patients: 2017 report A recent report (23) presented comparisons of 531 patients with RA *versus* 626 with OA from 4 rheumatology sites at which all patients with all diagnoses complete an MDHAQ at all visits in the waiting area before seeing the rheumatologist as part of routine care (24). The 4 sites were Liverpool Hospital in New South Wales, Australia, a public academic site; Rush University Medi-

cal Center in Chicago, IL, USA, a private academic site; NYU Hospital for Joint Diseases in New York, NY, USA, another private academic site; and Arthritis and Rheumatology, a solo private practice in Ridley Park, a suburb of Philadelphia, USA (23).

The 2-page MDHAQ includes 0-3 scores for physical function in 10 activities; the 0-30 total is divided by 3 for a 0-10 score. Two 0-10 pain and patient global assessment (PATGL) VAS are added to the 0-10 physical function score, compiled into a 0-30 routine assessment of patient index data (RAPID3) score. The MDHAO also includes a 0-10 fatigue VAS and a rheumatoid arthritis disease activity index (RADAI) self-report painful joint count, in which pain in 8 joint groups bilaterally is rated 0-3 (25). RADAI data may be reported as a total score of 0-48 or as a total count of joints rated as not painful or painful of 0-16. Rheumatologists estimate a 0-10 physician global assessment (DOCGL) VAS.

Median pain VAS scores were significantly higher in patients with OA compared to RA at all 4 sites (Table V), including 4.3 for RA versus 7.0 for OA at Liverpool, 5 for RA versus 7 for OA at Rush, 4.7 for RA versus 5.0 for OA at NYU, and 2.5 for RA versus 5.0 for OA at Ridley Park (p<0.001 at Liverpool, Rush, and Ridley Park, and <0.05 at NYU), adjusted for age, education, and disease duration (Table V). Other median MDHAQ scores for most variables were significantly higher in patients with OA compared to RA at 3 of the 4 sites, Liverpool, Rush, and Ridley Park, while similar in both diseases at NYU (Table V). Median RAPID3 scores were 9.7 for RA versus 16.8 for OA at Liverpool, 11.8 for RA versus 15.5 for OA at Rush, 11.0 for RA versus 11.7 for OA at NYU, and 6.2 for RA versus 12.2 for OA at Ridley Park (p<0.001 at Liverpool, Rush, and Ridley Park, and >0.05 at NYU), adjusted for age, education, and disease duration (Table V). Median RAPID3 indicated high severity (>12) in 3 of 4 OA groups versus moderate severity (6.1–12) in all 4 RA groups.

Median 0–10 VAS scores for fatigue ranged from 2.5–5 for RA and from 3.2-5 for OA, significantly higher in **Table V.** MDHAQ and DOCGL measures in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) at 4 clinical sites: Liverpool Hospital, Rush University Medical Center, NYU Hospital for Joint Diseases, and Ridley Park: El Haddad *et al.* 2017 (23).

	Liverpool Hospital		р	Rush Med	ical Center	р	NYU Ho Joint D	ospital for Diseases	р	Ridle	ey Park	р
	RA	OA	RA OA		RA	OA		RA	OA			
Number of patients	64	55	=	173	199	-	145	173	-	149	202	-
DHAQ: Patient Self-l	Report Meas	sures										
Function	1.7 (0.7-3)	3.3 (2.3-4.7)	<0.001	2.7 (0.7-3.7)	2.7 (1.3-4)	0.157	1.7 (0.3-3.7)	1.7 (0.7-3.3)	0.65	1 (0.3-2.7)	1.7 (0.7-3.3)	<0.001
Pain	4.3 (2.5-8.3)	7.0 (5.5-8.3)	<0.001	5 (2-7.5)	7 (5-8.5)	<0.001	4.7 (2-7)	5 (3-7.5)	0.03	2.5 (1-5)	5 (3-7.5)	<0.001
PATGL	4.3 (1.3-6.8)	6.0 (4.3-8)	0.002	4.5 (1.5-7)	5.7 (3.5-8)	<0.001	5 (1.5-7)	5 (2-6.5)	0.64	3 (1-5)	5 (3-7)	<0.001
RAPID3	9.7 (5.5-17)	16.8 (11.3-19.7)	<0.001	11.8 (4.3-18.7)	15.5 (10.2-19.5)	<0.001	11 (4-16.7)	11.7 (6.7-16.7)	0.28	6.2 (3-11.3)	12.2 (7.3-16.5)	<0.001
Fatigue	4 (1-7)	5 (2.8-8)	0.25	4 (1-7)	5 (2-7.5)	0.03	5 (0.5-8)	3.2 (1-7)	0.22	2.5 (1-5)	4 (1-6.5)	0.08
RADAI (0-48)	8 (3-15)	17 (10-2 2)	<0.001	7.5 (2-16)	10 (5-16)	0.11	5 (2-17.5)	6 (4-12)	0.48	7 (3-16)	8 (4-15)	0.08
RADAI (0-16)	5 (3-10)	10 (6-14)	0.01	6 (2-11)	6 (3-10)	0.79	5 (2-11.5)	4 (2-8)	0.66	6 (2-11)	6 (3-10)	0.80
RheuMetric: Physicia	un Global Es	timate										
DOCGL	4 (2-5)	5 (3-6)	0.039	3.7 (2-5)	4 (3.5-5)	0.036	2.5 (1.5-3.5)	2.5 (2-3.5)	0.14	1 (0-2)	2 (1-3)	<0.001

Values are median and interquartile range unless indicated otherwise, analysed by Mann-Whitney for non-normally distributed variables, *t*-test for normally distributed variables, chi square for qualitative variables. *p*-values according to MANOVA, adjusted by age, education level, and disease duration (when available). MDHAQ: multidimensional health assessment questionnaire; RAPID3: Routine Assessment of Patient Index Data 3; RADAI: Rheumatoid Arthritis Disease Activity Index; PATGL: patient global estimate; DOCGL: physician global estimate; RA: rheumatoid arthritis; OA: osteoarthritis.

OA only at Rush (p=0.03) (Table V). Median 0-48 RADAI self-report painful joint count scores ranged from 5-8 for RA and from 6-17 for OA from 3 settings. The number of affected joint groups (total=16) ranged from 5-6 in RA and 4–10 in OA (p<0.001 only at Liverpool, and >0.05 at Rush and NYU) (Table V). Median physician global estimates (0-10) ranged from 1-4 for RA and from 2-3 for OA at the 4 settings (Table V). This was the only report that included a measure from a health professional, which was consistent with the patient self-report questionnaire data.

Since patients with OA were older, mean levels of RAPID3 and its components were compared in a subset of patients age 55–70 with OA *versus* RA (Table VI). Mean physical function differed significantly only at Liverpool, but mean scores for pain, PATGL and RAPID3 were significantly higher (indicating poorer status in OA) at 3 of the 4 sites, all but NYU at which they were in a similar range (Table VI). These data indicate further that poorer status of OA patients compared to RA patients is not explained by higher age.

Discussion

The data presented in this review indicate that the burden of disease in patients with OA appears similar to patients with RA at this time, not explained by age, duration of disease, or patient formal education level. RA traditionally has been viewed as more severe than OA primarily on the basis of laboratory and radiographic findings, and this view remains held. It appears possible that functional status was more severe in RA than OA at earlier times, although pain VAS scores were higher in OA than RA in 1989 when physical function scores were higher in RA. RA appears clinically improved from earlier periods in recent years (26-30), in part due to earlier and new treatments (31, 32) and possible changes in the natural history (33).

Disease burden in OA often has been underestimated, as noted in previous reports (15, 16, 34-36). Even OA patients who reported "an impact on

work, leisure, social activities, and relationships described OA "as part of a normal aging process requiring acceptance, not treatment" (37). However, several reports which do not include formal comparisons with RA indicate that OA often has adverse consequences for individual patients and society (8-10, 38-40), including increased mortality rates in some (41-44), but not all, reports (45). One recent study indicates similar scores for physical function, pain, patient global assessment, and RAPID3 in OA versus RA at first visit, which were improved considerably more in RA versus OA at a subsequent visit two months later (35). Therefore, a hierarchy of RA being considerably more severe than OA pertains to laboratory findings but is not accurate concerning clinical status from a patient's perspective at this time.

The findings also add to the pragmatic and scientific rationale for all patients with all diagnoses to complete the same patient questionnaire at each visit (46). This practice provides the capacity to compare disease burden in OA *versus* **Table VI.** Mean MDHAQ scores for physical function, pain, patient estimate of global status, and RAPID3 composite scores, in patients age 55-70 with RA and OA at 4 clinical sites: Liverpool Hospital, Rush University Medical Center, NYU Hospital for Joint Diseases, and Ridley Park: El Haddad *et al.* 2017 (23)

	Liverpool Hospital		Hospital p Rus		Medical Center		NYU Hospital for Joint Diseases		р	Ridley Park		р
	RA	OA		RA	OA		RA	OA		RA	OA	
Number of patients	35	31	-	62	86	-	36	83	-	43	69	-
Age	62.5 (61.0-64.0)	62.1 (60.1-64.0)	0.721	62.2 (61.1-63.3)	62.6 (61.7-63.4)	0.648	62.2 (60.9-63.6)	63.2 (62.2-64.1)	0.266	60.4 (59.2-61.6)	63.1 (62.1-64.2)	0.001
Disease duration	11.1 (3.2-14.6)	6.0 (1.4-6.5)	0.01	N/A	N/A	N/A	N/A	N/A	N/A	10.3 (1.9-15.1)	6.3 (1.4-9.2)	0.03
Function	2.4 (1.6-3.2)	3.7 (3.1-4.3)	0.011	2.6 (2.1-3.1)	2.9 (2.4-3.3)	0.402	2.2 (1.5-2.9)	2.2 (1.8-2.6)	0.889	1.8 (1.2-2.3)	1.8 (1.4-2.2)	0.828
Pain	4.9 (3.9-5.9)	7.2 (6.4-7.9)	<0.001	5.0 (4.3-5.8)	6.4 (5.8-7.1)	0.005	4.8 (3.6-5.9)	5.3 (4.8-5.9)	0.316	3.2 (2.5-4.0)	4.8 (4.0-5.5)	0.005
PATGL	4.2 (3.2-5.2)	5.8 (4.8-6.8)	0.034	4.5 (3.8-5.3)	5.8 (5.2-6.5)	0.008	4.5 (3.4-5.6)	4.3 (3.7-5.0)	0.801	3 (2.2-3.8)	4.7 (4.1-5.3)	0.001
RAPID3	11.4 (8.8-14.0)	16.9 (14.8-19.0)	0.002	11.9 (9.8-14.1)	15.4 (13.5-17.2)	0.015	11.6 (8.8-14.4)	11.9 (10.4-13.3)	0.844	8.0 (6.1-9.9)	11.2 (9.7-12.8)	0.009

Values are means and 95% confidence intervals, p-values according to t-test.

MDHAQ: multidimensional health assessment questionnaire; RAPID3: routine assessment of patient index data 3; PATGL: patient estimate of global status; RA: rheumatoid arthritis; OA: osteoarthritis.

RA, or in all different rheumatic diseases. Although developed initially to assess RA (47), MDHAO/RAPID3 has been found informative in clinical care of patients with many rheumatic diseases (48), including systemic lupus erythematosus (SLE) (35), gout (35), ankylosing spondylitis (AS) (35, 49-52), and vasculitis (53), as well as OA (35, 54). Several limitations of this review and the studies therein should be noted. Different questionnaires were used to assess pain and function within different studies, although this may be viewed as desirable to recognise generalisability. Only a single cross-sectional visit is presented, and the data do not reflect possible changes from an initial visit and possible treatment effects which may have affected patient scores. Data concerning physical examination, radiographic findings, and laboratory studies are not available. The studies were undertaken between 1989 and 2017 and differences in the natural history of RA and OA and their treatment have occurred over the 3 decades. More detailed information on associations with sex, work status, secondary diagnoses, such as secondary OA in patients with RA and secondary fibromyalgia in patients with RA or OA, would add clarification to the findings. Nonetheless,

the data in the aggregate make a strong case that OA carries a severe disease burden for patients, comparable to RA. As noted, it is not appropriate to suggest that either OA or RA is "more severe" at a group or individual level. The composite evidence indicates that many patients with OA experience a severe disease burden in a similar range to patients with RA. These findings are not consistent with current teachings that RA is a more severe disease in general than OA, particularly in an era of major advances in available therapies for RA (31). Adjustment of the current approach to OA from both clinical and public policy perspectives appears indicated, including directing resources to research to improve therapies and outcomes in OA.

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Severity of osteoarthritis / J.R. Chua et al.

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