Osteoarthritis is as severe as rheumatoid arthritis: evidence over 40 years according to the same measure in each disease

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ABSTRACT

Osteoarthritis (OA) may be associated with substantial work disability, morbidity, costs, and increased mortality rates, often similar to rheumatoid arthritis (RA), documented in many published reports over the last 4 decades. However, OA generally has been viewed as less severe than RA. This discrepancy may be explained in part by:

a) RA may have been considerably more severe in the past, prior to effective therapies.

b) most older individuals have radiographic joint damage, which often is not associated with clinical symptoms.

c) RA is associated with abnormal laboratory tests, which are regarded as conveying greater significance than symptoms of pain and disability according to a "biomedical model," the dominant paradigm of modern medicine.

d) Most reports of OA and RA have emphasised differences between the 2 diseases even beyond laboratory abnormalities in pathogenesis, physical findings, and imaging.

e) Even pain and functional disability seen in both diseases are assessed using different patient self-report questionnaires, a WOMAC (Western Ontario McMaster Universities osteoarthritis index) in OA, and HAQ (health assessment questionnaire) in RA.

An identical measure is required for optimal direct comparisons, which has been used in 8 studies performed between 1979 and 2019 at 8 sites in North America, Europe, and Australia. These studies were primarily based on retrospective analyses at sites which collected a patient questionnaire in routine clinical care by all patients at all visits to inform clinical decisions. A pain visual analogue scale (VAS) was higher in OA compared to RA in 11/12 patient groups, while physical function on a HAQ (health assessment questionnaire) or derivative MDHAQ (multidimensional HAQ) and RAPID3 (routine assessment of patient index data) were slightly higher in RA before 2013 and higher in OA in later reports. Furthermore, a study of population-based data from the 1978 US Health Interview Survey indicated similar levels of disability and earnings losses according to surrogate variables for OA and RA.

Therefore, at least over the last 40 years, pain and functional disability in OA have appeared to be severe and similar to RA. These observations also illustrate the potential value of using an identical patient questionnaire in all patients at all visits in routine care settings, analogous to using the same laboratory tests such as erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) in all rheumatic diseases, and maintaining a database of the results for later analyses.

Introduction

Osteoarthritis (OA) has conventionally been viewed as a mild disease relative to rheumatoid arthritis (RA), which has served as a benchmark for severe arthritis. For example, the 2003 Bulletin of the World Health Organisation for the "Bone and Joint Decade 2000-2010" stated that "rheumatoid arthritis … is a more disabling disease … than lower limb osteoarthritis" (1). Even some patients being treated for OA in a rheumatology setting described OA in focus groups "as part of a normal aging process requiring acceptance, not treatment (What do you expect? You're just getting older)" (2).

Although the above comments reflect the "conventional wisdom" of the medical community and general public, they are not based on systematic analysis of disease burden. Many reports indicate that OA is associated with substantial morbidity (3), costs (4, 5), and increased mortality rates (6-9), suggesting that OA is indeed a severe

disease. However, most of the literature concerning OA and RA emphasises *differences* in pathophysiology, physical findings, imaging, laboratory tests, and treatments, rather than similarity of the 2 main symptoms, pain and functional disability. Assessment of pain and physical function requires a patient self-report questionnaire, and different instruments are used in most of the literature, a WOMAC (Western Ontario McMaster Universities Osteoarthritis Index) in OA (10) and HAQ (health assessment questionnaire) in RA (11).

We have identified 8 published reports in which identical patient questionnaire measures were used to compare disease burden of pain and physical function in patients with OA or RA over 40 years since 1979 (Table I). All 8 indicate that OA is not a mild disease. All but 1 report indicated higher pain visual analogue scale (VAS) scores in OA compared to RA. Four of 5 reports before 2013 indicated that RA patients had slightly higher scores (indicating poorer status) for physical function and RAPID3 (12) (a 0–30 index composed of 3 0–10 scores for physical function, pain and patient global assessment) than OA patients, but all 6 reports since 2017 indicated poorer physical function and RAPID3 scores in OA patients.

Patient self-report questionnaires traditionally have been regarded as "subjective," and less informative than high technology "objective" measures (13). While patient questionnaires cannot advance direct knowledge of pathophysiology, they provide validated quantitative data from the clinical encounter, which often is as informative as (or more informative than) laboratory tests and imaging data for clinical decisions (14, 15).

In RA, poor physical function, comorbidities, low socioeconomic status, and age are the most significant variables in the prognosis of work disability (16-19) and mortality (15, 20-25), substantially more significant than traditional markers of "poor prognosis RA," such as radiographs and laboratory tests (15-25). Poor physical function and comorbidities appear to be significant risk factors for mortality in OA (9, 26), similar to what has been well-described in RA, and consistent with data presented in this review that disease burden in OA is severe and similar to RA. Furthermore, the data also illustrate the potential value of using the same patient questionnaire measure in all patients seen in routine care settings, analogous to laboratory tests such as erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), for which identical measures are used in all rheumatic diseases, and maintaining a database for possible retrospective analyses.

This review summarises data from 8 reports concerning direct comparisons of OA and RA according to identical measures in 8 settings in London UK, Nashville TN USA, Wichita KS USA, Oslo Norway, New York NY USA, Philadelphia PA USA, Chicago IL USA, and Sydney Australia. It includes also analyses from a population-based US survey of individuals in 1978, prior to any of the clinical studies, which also suggest that OA is a severe disease, similar to RA. Some implications of these observations are discussed briefly.

Comparisons of patients with OA *versus* RA assessed in routine care using identical patient self-report questionnaires between 1979 and 2009

Eight clinical comparisons of OA *versus* RA between 1979 and 2009 are available in which quantitative data from identical self-report questionnaireswere completed by patients with either diagnosis (27-34) (Tables I, II, A3). These reports emerged from 8 clinical sites that were among the earliest to employ patient questionnaire completion in consecutive patients as a component of routine care. These sites were in London, UK (31), Nashville TN, USA (27, 30), Wichita KS, USA (28), Oslo, Norway (29), Ridley Park in suburban Philadelphia USA (32, 33), New York NY USA (32), Chicago IL USA (32, 34), and Liverpool Hospital Australia (32). Only 3 of the studies (29, 31, 33), involved a prospective design, and only 2 sought explicitly to compare OA to RA (29, 31). The remaining reports presented analyses of patient self-report questionnaire data that had been collected in routine clinical care and entered into long-term databases for possible retrospective studies.Two recent reports were directed specifically to compare OA to RA (32, 34) in retrospective analyses, while 4 studies had focused on properties of patient questionnaires; comparisons of OA *versus* RA had been incidental findings, which are presented to focus on observed similarity of OA and RA for this review (27, 28, 30, 33). All 8 studies included a pain visual analogue scale (VAS), although with different units; all results were normalised to 0–10 (Table I). All but 1 of 12 comparisons, in which pain VAS was 3.9 in both OA and RA, indicated a higher mean or median VAS score for OA compared to RA (Table I). Scores from the different sites cannot be compared directly – some are medians and others are means, and patients at the 8 sites differed according to socioeconomic status, duration of disease, and other variables. Nonetheless, scores appear relatively similar rather than different in the different sites, with ranges of 0–10 scores of 2.5–5.25 in RA and 3.86–7.0 in OA (inclusion of one or two decimals reflect what was reported) (Table I). Median values in RA were 4.7 in studies reported prior to 2013 and 4.3 instudies reported in 2017 and 2019, suggesting some improvement, while median values in OA were 4.32 in studies reported prior to 2013and 6.1 in 2017 and 2019, suggesting greater severity (Table I), although, as noted, these must be regarded as only approximate comparisons.

Seven of the 8 studies included a HAQ (28) or a derivative modified HAQ (MHAQ) (27, 35) or multidimensional HAQ (MDHAQ) (32-34, 36), all of which were reported after 1980, the year of publication of the HAQ (11); again, all scores are normalised to 0–10. Physical function scores in RA ranged from 1.9–4.09, median 3.2, in studies reported prior to 2013, and from 1.0–2.8, median 1.7, in studies reported in 2017 or 2019 (Table I). In OA, physical function scores ranged from 1.8–3.3, median 1.89, in reports prior to 2013 and 1.7–3.3, median 2.7, in reports in 2017 or 2019 (Table I). Again, the data are compatible with some improvement in RA and worsening in OA.

The studies that included a HAQ or

Table I. Pain visual analogue scale (VAS) and physical function scores in the rheumatology literature in patients with rheumatoid arthritis (RA) and osteoarthritis (OA).

Report	Pain VAS			Physical function HAQ*, MHAQ**, MDHAQ***		
	RA	OA	Poorer scores	RA	OA	Poorer scores
Huskisson*et al*. 1979 (31) – Pain VAS (adjusted from 0-20)	5.25	5.3	OA	NA	NA	NA
Callahan *et al*. 1989 (27)	5.16	6.01	OA	3.10**	1.86**	RA
Wolfe and Kong 1999 (28) (adjusted from 0-3)	3.66‡	4.32‡	OA	3.30*	3.30*	Equal
Pincus and Sokka 2007 (30)	4.70	4.52	OA	2.91***	1.89***	RA
Slatkowsky-Christensen, Mowinkel, Kvien. 2009 (29) HAQ (adjusted from 0-100)	3.64	3.86	OA	4.09*	3.03*	RA
Castrejon, Bergman, Pincus, 2013 (33)◊ 2-month follow-up visit	3.9	3.9	Equal	1.9***	1.8***	RA
El Haddad *et al*.2017 (32) median IQR						
Liverpool (Sydney) Australia	4.3	7.0	OA	1.7***	3.3***	OA
Chicago, USA	5.0	7.0	OA	2.7***	2.7***	Equal
New York, USA	4.7	5.0	OA	1.7***	1.7***	Equal
Philadelphia, USA	2.5	5.0	OA	1.0***	1.7***	OA
Chua *et al*.2019 (34◊						
6-month follow-up visit prior-DMARD RA	5.1	6.1	OA	2.8***	2.8***	Equal
6-month follow-up visit, DMARD-naïve RA	4.4	6.1	OA	1.6***	2.8***	OA

VAS: visual analogue scale; HAQ: health assessment questionnaire; MHAQ: modified HAQ; MDHAQ: multidimensional HAQ; SD: standard deviation; IQR: interquartile range DMARD: disease-modifying anti-rheumatic drug.
◊Two studies included baseline initial visits and follow-up visits. Only the follow-up visits are shown in this table, as the other studies did not include initial visits, but prospectively designed visits in 2 studies (29, 31) and random visits in routine clinical care in the others.
‡All mean or median scores for pain VAS and physical function were adjusted to 0–10.

MDHAQ physical function scale also included a patient global assessment of status and pain VAS, allowing calculation of RAPID3 (routine assessment of patient index data 3) (37), a 0–30 index composed of 3 0–10 scores for physical function, pain and patient global assessment (Table II). RAPID3 was the primary measure in recent reports in which disease burden was compared in patients with RA *versus* OA (32, 34). [RAPID3 was developed on the MDHAQ, but can also be calculated from the HAQ or any HAQ derivative]. RAPID3 has been found informative in all rheumatic diseases in which it has been studied, including OA (30, 38). In 3 studies reported prior to 2013 (27-29), RAPID3 results are "simulated," in that they are based on group scores rather than scores of individual patients (Table II).

RAPID3 scores were slightly higher in RA (indicating poorer status) in 4 of 6 comparisons reported prior to 2013, but higher in OA in all comparisons reported since 2013 (which may have included results over the previous decade) (Table II), although, as noted, comparisons of scores in many different settings are at best approximate. This finding would be consistent with developments in RA therapeutics over the last 2 decades, although differences might be less than expected, in view of dramatic increases in RA treatments and their costs between 1979 and 2019. There also is a trend toward worsening of OA (Table II), resulting in a greater disease burden in OA than RA according to RAPID3 in all groups reported since 2013 after treatment, on average, recognising substantial variation among individuals with either OA or RA.

Further descriptions of each of the studies are presented in an appendix, including data beyond a pain VAS, HAQ or MDHAQ physical function, and RAPID3 scores (Tables III-IV).

Analysis of a population-based survey data comparing disability and earnings in OA *versus* RA

The earliest direct comparison of OA *versus* RA known to the authors involved an analysis of work disability and earnings losses in the 1978 United States Health Interview Survey incorporated into the Social Security Survey of Disability and Work and reported in 1989 (39). This research was stimulated initially by a report of Yelin, Meenan, Nevitt, and Epstein in 1980 (16), which presented a new way of looking at RA as associated with frequent work disability, noting that "social and work factors combined had a far larger effect on work disability than all disease factors (16)." Another clinical study indicated that work disability was a severe outcome of functional declines over 9 years in an RA cohort reported in 1984 (21).

The population-based 1978 Social Security Survey of Disability and Work was studied to further analyse work disability and earnings losses in people with RA (17), in part to learn whether the clinical observations (16, 21) applied only to people with RA with unusually severe clinical status who were seen in rheumatology settings or might be more generalisable. A surrogate variable for RA termed "symmetric polyarthritis" was developed, defined as individuals age 18–65 (all study subjects were 18–65) who reported arthritis symptoms and a doctor's diagnosis of arthritis, as well as symmetrical pain or swelling in at least four joints, including at least two bilateral pairs, *e.g.* both hands and both knees. In order to analyse a "control" group of individuals with arthritis who did not have symmetric polyarthritis,

Table II. RAPID3 scores reported between 1989 and 2019 in RA and OA.

	RAPID3 RA	RAPID3 OA	n RA	n OA	Disease duration RA	Disease duration OA	Poorer status
Simulated group RAPID3 scores							
Callahan *et al*.1989 (27)¶	13.6	12.7	134	216	11.4	10.4	RA
Wolfe and Kong 1999 (28)¶	10.5	11.5	1013	655	9.2	16.9	OA
Pincusand Sokka (30), 2007*	12.1	10.4	280	39	NA	NA	RA
Slatkowsky-Christensen,Mowinkel, Kvien, 2009 (29)¶	11.7	11.0	194	190	18.8	10.7	RA
Castrejon, Bergman, Pincus (33), 2013							
Initial visit	12.6	12.4	39	41	3.5	6.1	RA
2-month follow-up visit	9.2	10.3					OA
El Haddad *et al*. 2017 (32)							
Liverpool (Sydney)							
Australia	9.7	16.8	64	55	6.7	4.4	OA
Chicago	11.8	15.5	173	199	NA	NA	OA
New York	11.0	11.7	145	173	NA	NA	OA
Philadelphia	6.2	12.2	149	202	6.9	3.9	OA
Chua *et al*. 2019 (34)							
Initial visit (prior-DMARD, DMARD-naïve)	15.5, 15.6	16.0	153, 50	149	3.2, 1.0	3.4	OA
6-month follow-up visit (prior-DMARD, DMARD-naïve)	12.5, 9.9	14.3					OA

¶Simulated group RAPID3 scores, rather than for individual patients *RAPID3 scores 0–10, adjusted to 0–30 used after 2008. ‡Recalculated from 0–10 scores in first report of RAPID3, although 0–30 scores have been used since 2008 to save 5 seconds in calculation of RAPID3. Two studies included baseline initial visits and follow-up visits (33, 34).

Table III. Disability status, work status, and earnings of women and men age 18–64 in 1978 US population with no arthritis, symmetric polyarthritis (a surrogate for rheumatoid arthritis) or asymmetric oligoarthritis (a surrogate for osteoarthritis).

	Total population	No arthritis	Symmetric polyarthritis	Asymmetric oligoarthritis
Women				
Total number (thousands)	64,012	51,520	1,511	2,687
% of population	100%	80.5%	2.4%	4.2%
Disability status				
% not disabled	82.2%	90.1%	22.2%	33.1%
% moderately disabled	8.1%	5.4%	26.8%	19.3%
% severely disabled	9.6%	4.5%	51.0%	47.5%
% Working	58.0%	61.6%	31.0%	35.5%
Earnings				
Annual income		$8,006	$2,122	$2,417
% of no arthritis			26.5%	30.2%
Earnings gap			$5,884	$5,589
Men				
Total number (thousands)	62,670	54,003	855	1,574
% of population	100%	86.2%	1.4%	2.5%
Disability status				
% not disabled	81.4%	90.6%	29.7%	28.6%
% moderately disabled	8.5%	5.8%	23.3%	26.9%
% severely disabled	7.2%	3.7%	47.0%	44.5%
% Working	87.1%	89.4%	56.1%	66.7%
Earnings				
Annual income		$19,360	$9,198	$12,194
% of no arthritis			47.5%	63.0%
Earnings gap			$10,162	$7,166

Source: developed from data reported on the 1978 Survey of Disability and Work, weighted to be representative of the U.S. working age population, age 18–64 (39).

a second variable, "asymmetric oligoarthritis," was defined as individuals who reported arthritis symptoms and a doctor's diagnosis of arthritis but had fewer than 4 involved joints and fewer than two symmetric pairs, regarded as a surrogate for OA.

This strategy identified 2.4% of women and 1.4% of men as having symmetric polyarthritis, the surrogate for RA, and 4.2% of women and 2.5% of men as having asymmetric oligoarthritis, the surrogate for OA (39) (Table III).The proportion of all survey respondents who reported "arthritis" was 11.3% (40), and the strategy identified 10.5% of all respondents(2.4+1.4+4.2+2.5=10.5), *i.e*. 93% of all survey subjects who reported arthritis. It is very likely that the proportion with RA was overestimated, based on a generally recognised prevalence of RA of 0.5%–1%, and the proportion of OA patients was underestimated (1). Many people with OA have symmetric polyarthritis involving at least 4 joints (9, 31, 32, 34, 41), who would have been misclassified as "symmetric polyarthritis" (or RA), rather than "asymmetric oligoarthritis" (or OA), as this phenomenon was not widely-recognised at the time.

The analyses indicated a high level of work disability in individuals with symmetric polyarthritis, the surrogate for RA (17), but also an unexpected observation that people with asymmetric oligoarthritis, the surrogate for OA, were almost as likely to be severely disabled and unlikely to be working as people with symmetric polyarthritis. Therefore, a more detailed study was initiated to compare work disability and earnings in individuals with symmetric polyarthritis *versus* asymmetric oligoarthritis (39).

The proportions of individuals with symmetric polyarthritis *versus* asymmetric oligoarthritis *versus* no arthritis who were not disabled were 22.2%, 33.1%, and 90.1% in women and 29.7%, 28.6%, and 90.6% in men, respectively; the proportion who were working in the three groups were 31%, 35.5%, and 61.6% in women and 56.1%, 66.7% and 89.4% in men, respectively (Table III). The proportions who reported themselves as severely disabled were 51.0%,

Table IV. Disability status and work status in individual age 18–64 according to number of joints with pain and swelling.

Number of joint problems	Estimated number of persons	Percent of working age population	Disability status			Work status
			Percent not disabled	Percent moderately disabled	Percent severely disabled	Percent working*
None	108,709	85.6%	89.3%	6.1%	4.6%	77.4%
One joint	5200	4.1%	62.4%	16.8%	20.8%	69.2%
Two joints	5522	4.3%	53.1%	22.2%	24.7%	69.2%
Three joints	1823	1.4%	47.1%	18.1%	34.8%	58.1%
Four joints	2041	1.6%	43.8%	23.2%	33.0%	62.7%
Five or six joints	1476	1.2%	28.6%	29.7%	41.7%	49.6%
Seven to nine joints	1017	0.8%	16.9%	27.9%	55.2%	38.9%
Ten or more joints	1259	1.0%	11.3%	27.6%	55.0%	39.0%

*Estimated number of persons working is reported because these numbers are not based on the total sample. Some Survey respondents did not indicate their work status.
Source: developed from data reported on the 1978 Survey of Disability and Work, weighted to be representative of the U.S. working age population, age 18–64 (39).

47.5% and 4.5% in women, and 47.0% 44.5%, and 3.7% in men, respectively (Table III) (39). The calculated earnings of women with symmetric polyarthritis was 26%, and of those with asymmetric polyarthritis was 30.2% compared to individuals with no arthritis (Table III). These proportions in men were 47.5% for those with symmetric polyarthritis and 63.0% in those with asymmetric oligoarthritis (Table III) (39).

Furthermore, the proportion who were disabled was directly proportional to the number of involved joints in all people with arthritis, regardless of whether they met criteria for symmetric polyarthritis or asymmetric oligoarthritis (Table IV) (39). Overall, 85.6% of the 18–64 US population indicated no pain, swelling, or stiffness of any joint, of whom 89.3% reported themselves as not disabled and only 4.6% considered themselves to be severely disabled; 77.4% of these individuals were working. By contrast, 20.8% of individuals reporting only a single involved joint were severely disabled, and only 69.2% were working. The 1.4% of the age 18–64 US population with 3 involved joints included 47% who were not disabled and 58% who were working. Of the 1.2% with 5 or 6 involved joints, only 28.6% were not disabled and 49.6% were working. The 1% with 10 or more involved joints included only 11.3% not disabled and 39% working *versus* 55.0% severely disabled (Table IV) (39).

These data are consistent with many observations that have extended knowledge concerning high rates of disability and earnings losses in people with OA or RA (4, 5, 42-46). One report estimated that OA and RA each accounted for costs involving 1% of the US gross domestic product (GDP), comparable to an economic recession (4). The number of involved joints appears more important in the likelihood of work disability than whether a person has RA or OA, although substantial disability and work compromise was seen in the presence of even a single involved joint (Table IV). Recent observations in OA also indicate that the number of hips and knees affected by symptomatic OA was the strongest determinant of walking difficulty (9).

Discussion

Data from 8 studies between 1979 and 2019 from 8 different rheumatology settings on three continents clearly indicate that patients with OA have a high disease burden, and that the burden is comparable to that in RA (Tables I-IV), notwithstanding extensive variation among settings according to socioeconomic status, duration of disease, and many other variables. WOMAC and HAQ pain and physical function scores are highly significantly correlated ($r>0.7$, $p>0.001$) in both RA and OA.

All reports found a severe disease burden in OA, with higher pain VAS in OA compared to RA in 11/12 patient groups, while physical function and RAPID3 scores were slightly higher in RA before 2013 and higher in OA in recent reports. Furthermore, a study of population-based data from the 1978 US Health Interview Survey indicated similar levels of disability and earnings losses according to surrogate variables for OA and RA.The data are compatible with slight improvement of RA and slight worsening of OA over 40 years, suggesting that OA may be more severe than in the past (47), although the absence of greater improvement in RA might be disappointing in light of the dramatic improvement in therapeutics and considerably higher costs for treating RA over this period.

In addition, data reported in 1989 from the 1978 US Health Interview Survey, designed to be representative of the US population, indicated substantial work disability and earnings losses in people identified with a surrogate variable for OA that were almost as severe as those identified with a surrogate variable for RA (Table I) (39). While the prevalence of OA likely was underestimated and that of RA overestimated by the strategies used to create surrogate variables, again, disability and income losses in the two groups were considerably more similar than different. Furthermore, the likelihood of disability appeared to increase according to the number of involved joints, regardless of diagnosis (Table II) (39).

The misperception of OA as generally mild compared to RA may be explained in part by several phenomena: First, it may be that RA was considerably more severe than OA before a truly disease-modifying anti-rheumatic drug became available with use of methotrexate in the 1980s (48, 49). Furthermore, some evidence suggests that RA may be becoming milder (50, 51), while OA appears more severe than in the past, even beyond the increased prevalence of an aging and more obese population (47). Nonetheless, even the population-based data from 1978 indicated a high level of work disability and earnings losses associated with OA that approached those of RA (39) and clinical data from 1979 indicated similar pain VAS scores in both diseases (31).

A second basis for underestimation of OA may have emerged from the universal radiographic joint damage observed during aging, which often is not associated with clinical symptoms (52). Many people with radiographic damage and/or mild symptoms never visit a physician for OA.These individuals are not included in clinical studies. Even most population-based studies include a query concerning a diagnosis of arthritis by a physician (39), so arthritis is not recorded in the study for anyone who has not visited a physician to receive such a diagnosis.

Much of the medical literature concerning OA must be viewed as pertaining primarily to individuals who have sought medical care for OA, though many people with symptomatic OA have indeed sought medical attention; in one study, a similar proportion of patients with OA and RA were referred by physicians rather than self-referred to a rheumatology setting (34).

A third basis for underestimation of OA may be that most reports concerning OA and RA have emphasised differences between the 2 diseases, in pathogenesis, physical findings, and radiographs, as well as laboratory abnormalities, rather than similar most prominent symptoms of pain and functional disability. Fourth, RA is associated with abnormal laboratory tests, which generally are regarded as conveying greater significance than symptoms of pain and functional disability according to a "biomedical model," the dominant paradigm of modern medicine (53).Finally, even the common most frequent symptoms of pain and functional disability in OA and RA generally are assessed using different patient self-report questionnaires, a WOMAC in OA (10), *versus* a HAQ in RA (11), making direct comparisons difficult. Nonetheless, as noted above, the only published analysis of the WOMAC and HAQ in RA and OA known to the authors indicated very high correlations (28), suggesting that either questionnaire could be used effectively to assess and monitor patients with either disease.

At the same time, it is somewhat puzzling that observations reported initially in 1979, and at least once a decade thereafter have remained largely unknown in the medical community. One possible explanation could be the trend beginning in the 1980s to consider clinical trials and other structured research as the as the primary (and often only) source of "evidence-based medicine" (54). This belief remains widespread despite recognition by experts in "evidence-based medicine" that, "While they are simple and easy to use, early hierarchies that placed randomised trials categorically above observational studies were criticised for being simplistic. In some cases, observational studies give us the 'best' evidence. For example, there is a growing recognition that observational studies – even case-series *and anecdotes* can sometimes provide definitive evidence (55)." Many limitations are seen to clinical trials (56-59), and valuable "evidence" can be learned from simple observations in routine care, as documented in this review.

From a medical perspective, the pathogenesis, diagnosis and treatment of RA and OA are quite distinct. By contrast, from the patient's perspective, RA and OA appear more similar than different. Similar patterns of MDHAQ/RAPID3 scores have been found in other rheumatic diseases with vastly different pathophysiologies and treatments, including systemic lupus erythematosus, ankylosing spondylitis, and gout, (see Fig. A1) (30, 33, 38).

One concern involves that most of the recent data presented are derived from MDHAQ/RAPID3 (Tables I-II). Nonetheless, comparisons according to the standard HAQ, WOMAC, AIMS2 and SF-36 (see Appendix Tables), as well as population-based data in which all subjects were studied according to a standard protocol (Table III), support the similarity of OA and RA.

Further studies will lead to increased capacity to use patient questionnaires to improve their value for clinical decisions and longitudinal analyses of disease course. Common clinical measurement tools in rheumatic diseases could become familiar to all rheumatologists and other physicians, analogous to blood pressure, haemoglobinA1C, ESR and CRP, to appreciate disease burden to the patient. It appears possible to develop a taxonomy of questionnaire findings in different rheumatic diseases in the 21st Century for different rheumatic diseases, analogous to the taxonomy of laboratory and radiographic findings that was developed in the 20th-century.

The clinical data summarised here required an identical measure to compare patients with OA and RA, which is unusual in the medical literature. Furthermore, a database of questionnaire responses was prerequisite for the analyses. Every patient encounter provides an opportunity to record patient questionnaire data, which can be of considerable value in clinical care, estimating prognosis, monitoring responses and adverse events with therapies, and documenting long-term outcomes if a database is established. Yet such opportunities are lost thousands of times every day in most rheumatology encounters. Perhaps further lessons learned from patient-reported data in routine clinical care will lead to more adoption of completion of a questionnaire by all patients, particularly as the patient does most of the work.

In summary, data compiled over the last 40 years from 8 different rheumatology settings, as well as population-based survey data, indicate considerable similarity in groups of patients with OA or RA.These observations appear to conflict with traditional views, but are supported by an extensive literature documenting the severity of OA. Much of this information requires the use of patient questionnaire-derived data. Simple databases are easily established using modern computer technology, and have the potential to provide information important to individual clinical decisions, as well as to understanding the effects of disease in patient populations.

Appendix

Further descriptions of each of the studies are presented in an appendix, including data beyond a pain VAS, physical function, and RAPID3 scores (Tables A1-A3, Figs. A1, A2).

a. London, UK, 1979

A study reported in 1979 from London UK compared 100 patients with OA *ver-*

Table A1. Comparison of individual measures other than pain visual analogue scale (VAS) scores in the rheumatology literature prior to 2017 in patients with rheumatoid arthritis (RA) and osteoarthritis (OA).

	RA	OA	*p*-value	Poorer scores
Huskisson *et al*. 1979 (31)				
Pain VAS (adjusted from 0-20)	5.25	5.3	Not given	OA
Duration of morning stiffness (mins)	58.2	22.5	Not given	
Duration of inactivity stiffness (mins)	7.1	8.0	Not given	
Callahan *et al*.1989 (27)				
MHAQ - Function‡	3.10	1.86	<0.001	RA
MHAQ – VAS Pain	5.16	6.01	<0.001	OA
MHAQ – Global Estimate‡	5.30	4.76	0.008	RA
Wolfe and Kong 1999 (28)				
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 (2.50)	3.30 (2.33)	--	=
VAS Pain (range 0-3) (SD)‡	3.66 (2.53)	4.32 (4.63)	--	OA
Patient global severity (range 0-100-adjusted to 0-10) (SD)	3.58 (2.40)	3.87 (2.44)	--	OA
Pincus and Sokka 2007 (30)				
MDHAQ – Function	2.91	1.89		RA
MDHAQ – VAS Pain	4.70	4.52		OA
MDHAQ – Global Estimate	4.45	3.99		RA
Slatkowsky-Christensen *et al*. 2009 (29)				
AIMS2 Physical	2.38	1.74	<0.001*	RA
SF-36 Physical Scale$^{\Delta}$	47.9	58.30	<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 adjusted to 0-10	3.64	3.86	0.35	OA
AIMS2 Pain	4.83	5.52	0.006*	OA
SF-36 Pain Scale$^{\Delta}$	43.70	40.40	0.11	OA
VAS Fatigue	50.40	44.20	0.04	RA
SF-36 Vitality$^{\Delta}$	42.90	41.00	0.40	OA
VAS Global	39.40	40.60	0.63	OA
SF-36 General$^{\Delta}$	46.20	52.80	0.005*	RA

*Statistically significant (<0.014 after adjustment for multiple testing by Sime's procedure).
‡Transformed to 0-10 to compare with MDHAQ scores.
$^{\Delta}$Higher score indicates better status, unlike other measures for which higher score indicates poorer status.

sus RA. VAS pain scores (adjusted from 0–20 to 0–10) were 5.3 in OA and 5.25 in RA (31) (Table I).Duration of morning stiffness was 22.5 minutes in OA and 58.2 minutes in RA, while "duration of inactivity stiffness" was 8.0 minutes in OA and 7.1 minutes in RA (Table A1). The authors commented that "osteoarthritis was usually a poly-articular disease and as symmetrical in distribution as rheumatoid; the knees and hands were the most commonly involved sites (31)."They concluded that the disease burden in OA was similar to that in RA, a phenomenon rediscovered every decade according to reports in this review.

b. Nashville, TN, USA, 1989

An early comparison of 216 OA patients and 134 RA patients was reported in 1987 (27) from Nashville, TN, using a modified health assessment questionnaire (MHAQ) (35), an interim version derived from the HAQ (11) in development of the MDHAQ (36, 60, 61).The study involved a retrospective analysis of data collected in consecutive patients in the clinic, designed to document the value of the MHAQ in in all rheumatic diseases for routine care, without a specific focus to compare results in OA *versus* RA. Patient global estimate was 5.30 in RA and 4.76 in OA (Table A1), higher in RA, as were physical function scores and RAPID3, while the pain VAS was higher in OA. The data suggest that RA may have been slightly more severe than OA in 1989, but the disease burden in OA clearly was substantial.

c. Wichita, KS, USA 1999

A study from Wichita by Wolfe and Kong in 1999 (28) reported comparisons of 655 OA and 1,013 RA patients according to both the HAQ (11) and WOMAC (10), the "gold standard" OA-specific assessment instrument for decades. The report analysed measurement properties of the HAQ and WOMAC questionnaires data collected in routine clinical care, and did not focus on possible differences between OA and RA. Nonetheless, this report presents the only analyses known to the authors in which OA and RA patients were compared according to both a HAQ and WOMAC, each of which includes a score for pain and for physical function.

WOMAC function was correlated with HAQ function at r=0.78 in both RA and OA patients, and WOMAC pain with HAQ VAS pain at r=0.73 in OA and 0.71 in RA (28). These correlations are quite high for any two clinical measures [for reference, a correlation of erythrocyte sedimentation rate (ESR) with C-reactive protein (CRP), two biomarkers that are often used interchangeably in RA clinical trials is 0.50 (62)]. Significant correlations of WOMAC function and pain scores support the validity of comparisons of patients with OA or RA by either a WOMAC or HAQ or derivative MDHAQ, which are optimally pursued using the same quantitative patient questionnaire measure.

Higher scores on the WOMAC were seen in patients with OA than RA in 4 of the 5 measures (Tables I, A1); simulated RAPID3 scores were 11.5 in OA and 10.5 in RA (Table II). Higher scores on the WOMAC might be anticipated in OA, which emphasises lower extremity function more than the HAQ. Nonetheless, HAQ physical function scores were similar in OA and RA, as in other studies (Table I), and the overall patterns were similar to the other studies in this review.

d. Nashville, TN, 2007

A review in 2007 of 39 OA patients *versus* 280 RA patients seen in Nashville between 1996 and 2005 was again directed to document the clinical value of MDHAQ/RAPID3 scores in all rheumatic diseases, and not specifically to compare OA to RA (30). Actual adjusted (although retrospective) RAPID3

Table A2. Median MDHAQ (multidimensional health assessment questionnaire) measures for physical function, pain, patient estimate of global status, as well as RAPID3 composite scores, fatigue, rheumatoid arthritis disease activity index (RADAI) self-report joint count 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. Source: ref. (34).

	Liverpool Hospital		*p*	Rush Medical Center		*p*	NYU Hospital for Joint Diseases		*p*	Ridley Park		*p*
	RA (n=64)	OA (n=55)		RA (n=173)	OA (n=199)		RA (n=145)	OA (n= 173)		RA (n=149)	OA (n=202)	
MDHAQ: Patient Self-Report Measures												
Function (0-10)	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 (0-10)	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 (0-10)	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 (0-30)	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 (0-10)	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

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 squared 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.

Table A3. Mean RAPID3 and component scores at initial visit, 6-month follow-up visit, and difference between initial and 6-month follow-up visits of patients with osteoarthritis (OA), rheumatoid arthritis (RA) with prior treatment, or treatment-naïve RA seen at Rush University Medical Center. Source: ref. (34).

Variable(s)	OA (n=149)			RA (n=203)					
				Prior treatment (n=153)			Treatment naïve (n=50)		
	1st visit	6 months	Difference	1st visit	6 months	Difference	1st visit	6 months	Difference
RAPID3 (0-30) unadjusted mean (SD)	16.0 (5.8)	14.3 (6.2)	-1.7 (5.2)***	15.5 (7.6)	12.5 (7.7)	-3.0 (6.8)***	15.6 (5.9)	9.9 (7.6)	-5.7 (7.0)***
RAPID3 (0-30) adjusted Mean (95%CI)	15.0 (12.9, 17.1)	13.3 (11.2, 15.3)	-1.7 (-3.8, 0.4)	15.8 (14.3, 17.2)	10.8 (8.5, 13.1)	-4.3 (-6.6,-1.9)	15.7 (13.5, 17.9)	10.3 (7.9, 12.7)	-5.7 (-8.2,-3.3)
Function (0-10) unadjusted mean (SD)	3.0 (1.9)	2.8 (1.9)	-0.2 (1.3)*	3.2 (2.4)	2.8 (2.3)	-0.4 (1.6)***	2.9 (2.1)	1.6 (1.9)	-1.2 (2.1)***
Function (0-10) adjusted mean (95%CI)	2.7 (2.1, 3.3)	2.4 (1.8, 2.9)	-0.3 (-0.9, 0.2)	2.7 (2.0, 3.4)	2.2 (1.6, 2.8)	-0.5 (-1.1,0.1)	3.4 (2.6, 4.1)	2.1 (1.6, 2.8)	-1.3 (-1.9,-0.7)
Pain (0-10) unadjusted mean (SD)	7.0 (2.2)	6.1 (2.6)	-0.9 (2.3)***	6.3 (3.0)	5.1 (3.1)	-1.2 (3.1)***	6.8 (2.5)	4.4 (3.3)	-2.4 (3.1)***
Pain (0-10) adjusted mean (95%CI)	7.0 (6.2, 7.8)	6.0 (5.1, 6.8)	-1.1 (-2.0,-0.1)	6.2 (5.3, 7.1)	4.5 (3.6, 5.5)	-1.7 (-2.7,-0.6)	6.6 (5.7, 7.7)	4.3 (3.3, 5.3)	-2.4 (-3.5,-1.3)
Patient global (0-10) unadjusted mean (SD)	5.9 (2.7)	5.4 (2.8)	-0.5 (3.0)*	6.0 (3.1)	4.6 (3.0)	-1.3 (3.2)***	5.9 (2.8)	3.9 (3.3)	-2.1 (3.5)***
Patient global (0-10) adjusted mean (95%CI)	5.3 (4.4, 6.2)	5.0 (4.1, 5.8)	-0.3 (-1.1, 0.7)	6.2 (5.2, 7.2)	4.1 (3.1, 5.1)	-2.1 (-3.2,-0.9)	6.0 (5.0, 7.1)	4.0 (2.9, 5.0)	-2.0 (-3.2,-0.8)

Values are the mean (standard deviation) for unadjusted and mean (95% confidence interval) inadjusted analyses for age, race, body mass index, level of formal education, and disease duration.
MDHAQ: Multidimensional health assessment questionnaire; RAPID3: Routine assessment patient index data 3. For differences from initial to 6 month visit ***$p<0.001$, **$p<0.01$, *$p<0.05$.

scores were 10.4 in OA *versus* 12.1 in RA (Table II) (30). Among RAPID3 components, higher scores for physical function and patient global assessment were seen in RA (Tables I, A1), while higher scores for pain were seen in OA (Table I), as in the previous study from Nashville (27).

e. Oslo, Norway 2009

A thorough comparison of 190 OA patients *versus* 194 RA patients was reported by Slatkowsky-Christensen, Mowinckel, and Kvien from Oslo in 2009 (29). This study was one of the two in this review which was designed prospectively to compare OA to RA [the other was Huskisson *et al*. (31)], and in-

cluded data from the HAQ (11), MHAQ (35), HAQ (11), SF-36 (63, 64), a generic questionnaire used in studies of many diseases, and AIMS2 (arthritis impact measurement scales-2) (65, 66), an "arthritis-specific" questionnaire modelled on the SF-36 (Table I, II, A1). Scoring of the SF-36 differs from most commonly used questionnaires in that higher scores denote better clinical status.

The OA patients in the Oslo study were selected for OA of the hand (29), and lower scores might be anticipated in patients with OA of the hands compared to OA involving lower extremities. However, 9% also had met criteria for hip OA and 59% of the patients had met criteria for knee OA (67). Pain scores by 3 different measures, VAS on the HAQ and MHAQ (Tables I, A1), AIMS2, and SF 36 were higher in OA *versus* RA, although HAQ function scores were higher in RA than OA, indicating poorer function in the RA group (Table A1). Simulated RAPID3 scores were 11.0 in OA patients and 11.7 in RA patients (Table II), within one unit on a 0–30 scale.

f. Comparison of RAPID3 at initial visit and 2 month follow-up visit in OA *versus* RA in Ridley Park (Philadelphia), 2013

A study was conducted in a private practice in suburban Philadelphia (Ridley Park) Pennsylvania, at which all patients complete MDHAQ/RAPID3 at each visit in routine care, to analyse RAPID3 scores at first visit and 2 months later in all patients with all diagnoses between December 2007 and March 2011 (33). Tables I, II, A1 and Figure A1 present retrospective analyses of 41 OA patients and 39 RA patients from the study that again was designed to recognise the value of the MDHAQ in documenting changes in clinical status from an initial visit to a subsequent visit 2 months later in routine clinical care of many diseases. Only the follow-up visit is depicted in Table I since the data in the other studies [(other than Chua *et al*. 2019 (34)] were not from the initial visit.Mean RAPID3 scores were slightly higher in RA than OA at first visit, but improved by 27.5% in RA *versus* 16.8% in OA (Table A1, Fig. A1) explained by better treatments for RA.Improvement was similar to RA in systemic lupus erythematosus (SLE) and gout, and similar to OA in spondyloarthropathies (Fig. A1) (33).

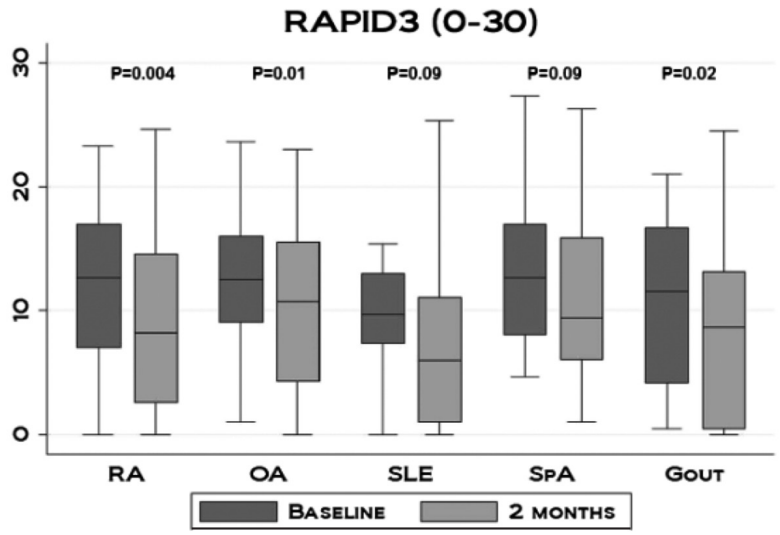

Fig. A1. Median, interquartile range, and limits of 95% confidence interval for RAPID3 score in patients with RA (n=39), OA (n=41), SLE (n=14), SpA (n=23), and gout (n=24), at baseline and 2 months later. P, repeated-measures t test (changes in RAPID3). Source: ref. (33).

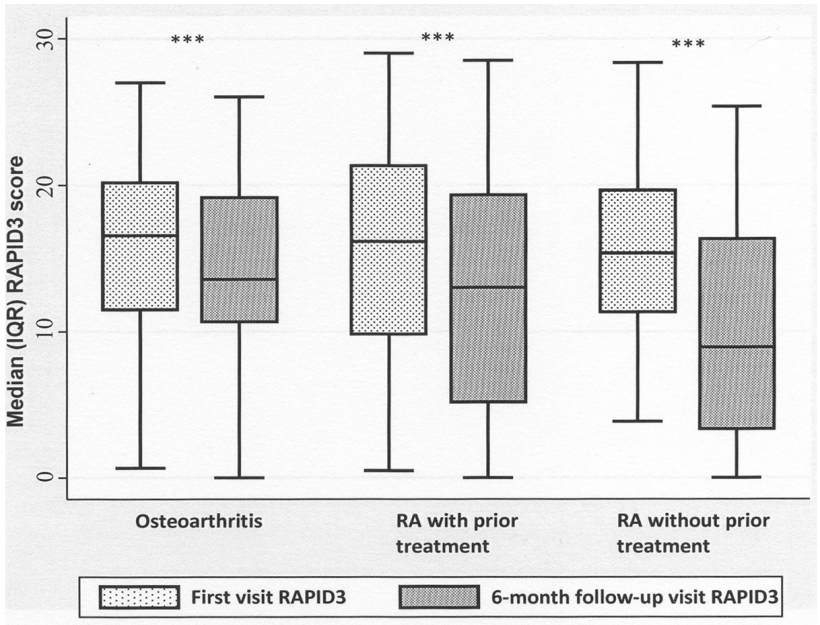

Fig. A2. Median (IQR) RAPID3 scores at first visit and 6-month follow-up visit for OA and RA with and without prior treatment seen at Rush University.
***$p<0.001$. Source: ref. (34).

g. A cross-sectional comparison of patients with OA and RA from 4 different settings in which MDHAQ is used in all patients in routine care, 2017

A comparison of disease burden in OA *versus* RA was stimulated by Dr Carlos El Haddad at Liverpool Hospital in Sydney Australia, and conducted as a cross-sectional retrospective analysis at 4 different rheumatology sites at which an MDHAQ/RAPID3 is assessed in each patient at each visit (32). Analyses were possible at these sites, as each site maintained a database of MDHAQ scores for subsequent longitudinal analyses.

Median pain VAS and RAPID3 were higher in OA *versus* RA at all four sites (Tables I, II, A2). Median physician global assessment at the 4 sites was

similar in OA *versus* RA (32), although physician global assessments were lower than patient global assessments in both diseases, but discordance is greater in OA than RA (68). Patterns were similar for individual RAPID3 items of physical function, pain, patient global assessment, as well as for fatigue, and RADAI (rheumatoid arthritis disease activity index) painful joint scales (69) on the MDHAQ (Table A2) (32).

h. Disease burden at one rheumatology setting is similar in OA and RA at initial visit but significantly greater in OA 6-months later, 2019

The background of cross-sectional evidence of greater disease burden in RA compared to OA at 4 sites (32) and relatively similar status of RA and OA patients at initial visit while OA patients had poorer status 2 months later (33) led to a larger study at Rush University in Chicago of patient status at initial and 6 month follow-up visits to compare disease burden in 149 patients with OA *versus* 203 with RA (34). Although the proportions of physician-referred patients were about 80% in each group, one unexpected complexity was that 153 of the 203 RA patients had already been treated with disease-modifying anti-rheumatic drugs (DMARDs) prior to their first visit to Rush University (34). Therefore, analyses were conducted in 3 groups: OA patients, RA patients who were "treatment-naïve," and RA patients who had "prior-treatment." All analyses were adjusted for age, body mass index (BMI), duration of disease, formal education level, and race. OA patients had slightly poor status initial visit, but the difference increased considerably at the 6 month visit (Tables I, II, A3, Fig. A2) (34). The change of RAPID3 from 15.6 to 9.9 (5.7 units) in treatment naïve patients clearly is higher than the minimal clinically important improvement (MCII) of RAPID3 of 3.8 (70).

Competing interests

T. Pincus holds a copyright and trademark for "MDHAQ" and "RAPID3," for which royalties and license fees are received from profit-making organisations by Medical History Services LLC, of which he is president. All royalties and license fees are applied to support further development of quantitative measurement using patient and physician questionnaires in routine clinical rheumatology care and research.

Y. Yazici has received research support from BMS, Celgene, Genentech, is a consultant for Celgene and Sanofi, and Chief Medical Officer of Samumed.

M. Bergman has received speaker fees from Abbvie, Celgene, Novartis and Sanofi; consultation fees from Abbvie, BI, Genentech/Roche, GSK, Horizon, Janssen, Novartis Pfizer and Sanofi; and holds stock in JNJ.

J.A. Block has received consultancy fees from Discgenics, GlaxoSmithKline, Medivir and Zynerba PHarma.

The other co-authors have declared no competing interests.

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