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ORIGINAL RESEARCH

A 5-Year Retrospective, Observational Study Assessing Rheumatoid Arthritis Disease Outcome Measures to Characterize Systemic Lupus Erythematosus Burden in the USA

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ABSTRACT

Introduction: We evaluated the use of rheumatoid arthritis (RA) disease measures in patients with systemic lupus erythematosus (SLE) in a US community-based rheumatology physician network over 5 years.

Methods: This retrospective, observational cohort study (GSK Study 213818) of patients with SLE utilized electronic medical records (01 January 2010–31 December 2019) from the United Rheumatology Normalized Integrated Community Evidence database. The index was the date of first SLE diagnosis recorded in the database; the observation period was 5 years post-index. RA disease measures evaluated were: Pain Index, Multi-Dimensional Health Assessment Questionnaire (MD-HAQ), Patient Global Assessment (PtGA), Physician Global Assessment (PGA), Swollen Joint Count (SJC), Tender Joint Count (TJC), Routine Assessment of Patient Index Data 3 (RAPID3), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), and Disease Activity Score 28 (DAS-28). The number of patients with measures utilized, the score on each measure, and proportion of patients per disease activity category were assessed.

Results: Overall, 5990 patients with SLE were included. The most frequently used measures were Pain Index, SJC, TJC, MD-HAQ, PtGA, RAPID3, and PGA (cumulative use over Years 1–5: 23.9–71.3%). For all measures, frequency of use was lowest in Year 1, followed by a general increase from Year 1 to Year 5. Scores remained relatively stable for most measures, and the proportion of patients in remission or with low/moderate disease activity per RAPID3 increased.

Conclusion: RA disease measure utilization in SLE was generally infrequent but increased over time. Pain Index and MD-HAQ were the most commonly applied cumulatively across 5 years of follow-up. The rationale for the increased use of these measures in SLE over time requires

Shirley P. Huang and Carlyne M. Averell are at the time of the study.

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further exploration. In the absence of a clinically applicable SLE-specific measure, the use of RA measures, for example in conjunction with SLE measures, may provide an alternative approach for measuring disease activity, representing an opportunity to improve patient outcomes.

Keywords: Autoimmune diseases; Disease activity; Outcome measures; Real-world study; Rheumatoid arthritis; SLE; Systemic lupus erythematosus

Key Summary Points

Why carry out this study?

Measurement of disease activity and its impact on a patient's life is important in systemic lupus erythematosus (SLE) owing to the heterogeneity in symptoms and organ systems involved in this disease, and its unpredictable relapsing–remitting nature.

Although SLE-specific disease measures such as the Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI) and the British Isles Lupus Assessment Group (BILAG) are commonplace in clinical trials, these are not used routinely in clinical practice.

What was learned from this study?

We assessed the use of rheumatoid arthritis (RA) disease measures in a large sample of patients with SLE in clinical practice over 5 years, since these measures are often employed in rheumatology practices.

In our study, the use of RA disease measures to assess patients with SLE was generally infrequent but increased over time. Despite the fact that they are not SLE-specific, combining RA disease measures with SLE-specific measures may aid the delivery of patient-centric care by contextualizing clinical laboratory measures of disease activity.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting multiple organ systems, and is associated with significant morbidity and mortality [1–3]. Common symptoms include fatigue, joint pain and swelling, weakness, and muscle pain [4]. More severe manifestations include cutaneous, neuropsychiatric, pulmonary, and hematological disease, and in particular, renal disease, which all have a significant impact on patients' health and quality of life [1, 5].

Currently there is no definitive diagnostic criteria for SLE, with the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) instead providing a set of classification criteria requiring at least one positive antinuclear antibody test as a mandatory entry criterion and additive criteria grouped in seven clinical (constitutional, hematologic, neuropsychiatric, mucocutaneous, serosal, musculoskeletal, renal) and three immunologic (antiphospholipid antibodies, complement proteins, SLE-specific antibodies) domains, each weighted from 2 to 10 [6]. Patients achieving $\geq$ 10 points are classified as having SLE [6].

SLE management options include antimalarials, corticosteroids, and immunosuppressants, which aim to improve symptoms and/or prevent disease flares, although prolonged use of corticosteroids can lead to organ damage [5]. Targeted biologics, such as belimumab and anifrolumab, treat the underlying cause of the disease and reduce the risk of damage while controlling disease activity and risk of flares [5, 7].

Despite these available treatment options, management of SLE remains challenging due to its unpredictable, relapsing–remitting nature and the diversity of symptoms and organ systems involved [4, 5, 7]. Optimal management of a patient with SLE requires comprehensive and regular assessments focused on disease activity and organ damage, in conjunction with laboratory tests, patient history, and physical examinations, to generate a comprehensive treatment plan [7–9]. However, clinical

assessments alone may not fully capture the impact of SLE on patients' lives, and the discordance between such assessments and how the patient truly feels contributes to the challenge of managing SLE [10, 11].

Several measures are available to evaluate disease activity, including lupus low disease activity state and associated organ damage in patients with SLE. These include the Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI), the British Isles Lupus Assessment Group (BILAG), the Physician Global Assessment (PGA), and the Systemic Lupus International Collaborating Clinics (SLICC)/ACR Damage Index (SDI) [7, 9, 11].

There is no consensus on which SLE disease measures should be used, although the convention is for more than one to be applied, and EULAR recommends that PGA is included in this selection [5, 12, 13]. For example, a real-world observational study of belimumab treatment in SLE included SELENA-SLEDAI, BILAG, and PGA to assess disease activity [14]. However, while standard in clinical trials and other clinical research settings, these tools do not appear to be used routinely in real-world clinical practice, possibly owing to their administrative burden, which may include a delay in scoring while awaiting imaging or laboratory test results, and/or the need for a physical examination [8, 12, 15]. Further, these measures (in addition to the reliance on laboratory tests) tend to focus on capturing or quantifying disease activity as opposed to measuring how the patient feels, two aspects of SLE that are not always in concordance [10, 11]. Ultimately, this may hinder the physician–patient relationship, as physicians feel progress is being made with improvements in clinical measures and laboratory results; however, patients feel discouraged as their well-being (e.g., pain, fatigue, and emotional distress) has not improved [11]. As such, clinical studies in SLE have more recently included measures of patient-reported quality of life as outcomes [11, 16].

Interestingly, rheumatoid arthritis (RA) disease measures, such as the Routine Assessment of Patient Index Data 3 (RAPID3), have been used by some physicians to assess patients with SLE; thus providing insight into the impact of SLE on patients' lives [8–11, 15, 17, 18]. The RAPID3 index is a quick and easy-to-use measure as it can be calculated in 5–10 s using scores from the three patient-reported domains of the ACR core dataset measures (physical function, pain, and patient global estimate of status) [19]. Importantly, RAPID3 has been shown to be a valid and reliable measure of health status in SLE [11, 19].

Other RA disease measures include the Swollen Joint Count (SJC), Tender Joint Count (TJC), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), and Disease Activity Score 28 (DAS-28), as well as more widely applied measures that have been adopted in RA including the Pain Index, Multi-Dimensional Health Assessment Questionnaire (MD-HAQ), Patient Global Assessment (PtGA), and PGA [20–25]. However, the clinical utility of these measures in monitoring disease activity in SLE has not been assessed.

The aim of this study was to retrospectively evaluate the use of RA disease measures in patients with SLE in a community-based rheumatology physician network in the USA, over a 5-years follow-up period.

METHODS

This was a real-world, retrospective, observational cohort study (GSK Study 213818) to describe the RA disease measures used for assessing patients with SLE over the 5-year observation period following the first record of an SLE diagnosis by a rheumatologist in the United Rheumatology Normalized Integrated Community Evidence (UR NICE) database.

Ethics

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. No direct patient contact or primary collection of individual human data (IHD) took place; the IHD was not owned by GSK, but its use aligned with the "purpose of use" outlined in the source contract and/or the terms and conditions of use of the data source

and complies with any specified prohibitions of use. Study results omitted patient identification, therefore informed consent and ethics committee or institutional review board approval was not required.

Data Source

Data were extracted from the UR NICE database, from 1 January 2010 to 31 December 2019 (Fig. 1). The UR NICE database is the largest clinical data repository on autoimmune disease sourced from electronic medical records in the USA and contains longitudinal data for > 1.8 million patients [26]. Data for all patients seen by a rheumatologist in the UR NICE network are captured in the database, along with electronic medical records from > 300 independent physician practices.

Study Design

The index date was defined as the date of the first diagnosis of SLE by a rheumatologist recorded in the UR NICE database between 1 January 2010 and 31 December 2014. The observation period was defined as the 5-year period following the index date, divided into 1-year increments.

Patients

Patients included in the study were required to be ≥ 5 years of age at the index date, have at least one diagnosis of SLE [i.e., International Classification of Diseases—9th Revision—Clinical Modification (ICD-9-CM) codes: 710.0x] between 1 January 2010 and 31 December 2014, and have ≥ 5 years of clinical activity (defined as the presence of physician services, such as clinical and laboratory measures, prescriptions, diagnoses, and procedures, in the database) post-index.

Study Variables

The RA measures evaluated were the Pain Index, MD-HAQ, PtGA, PGA, TJC, SJC, RAPID3, DAS-

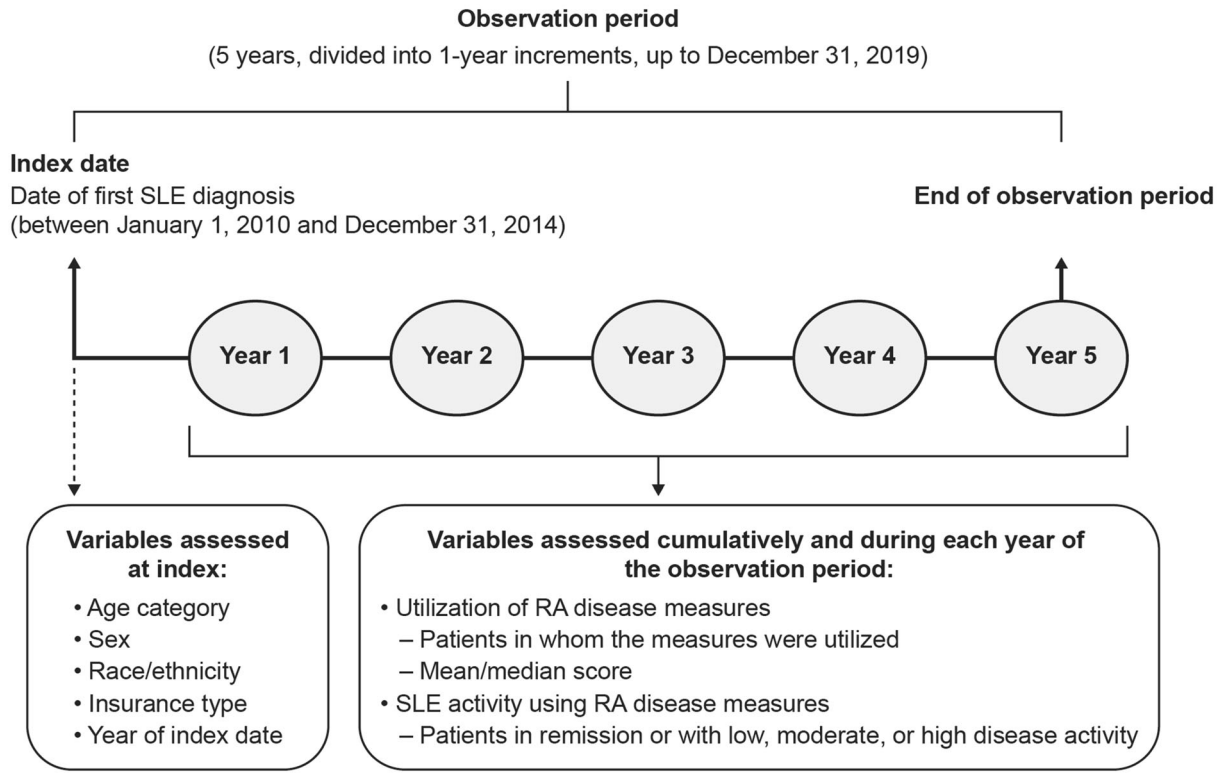

Fig. 1 Study design. *RA* rheumatoid arthritis, *SLE* systemic lupus erythematosus

28, CDAI, and SDAI (Table S1). Pain Index refers to a simple pain rating visual analog scale (VAS) completed by the patient, typically using a 0–10 scale with higher numbers denoting worse pain [27]. HAQ measures patient-perceived disability, discomfort, and pain, and medication side effects, as well as cost of care, and mortality [28]. MD-HAQ is derived from the HAQ to incorporate ten individual quantitative scores for physical function, fatigue, pain, global status, anxiety, sleep quality, morning stiffness, anxiety, exercise status, and change in status [29]. The MD-HAQ has a raw score from 0 to 30, and an adjusted final score from 0 to 10, with higher scores signifying worse health status [29]. PtGA and PGA utilize a simple VAS measuring overall disease activity based on the impact of disease on the patient and are completed by the patient and physician, respectively. Both measures are typically scored 0–10, with higher scores denoting higher disease activity [30]. TJC and SJC are scores based on the physical examination of 28 joints and therefore determined by the physician, with scores ranging from 0 to 28 [30]. RAPID3 is a brief patient-administered questionnaire on RA symptoms, and includes MD-HAQ, a pain VAS, and the PtGA. It has a raw score ranging from 0 to 30, which is then converted to a score of 0–10 [19, 30]. CDAI and SDAI are composite indices of 28-count SJC, 28-count TJC, PtGA, and PGA [and laboratory measurement of C-reactive protein (CRP); SDAI only] [20]. CDAI is scored 0–76.0, while SDAI is scored 0–86.0 [20, 30]. Finally, DAS-28 is a composite index measuring disease activity that comprises measures of 28-count SJC and 28-count TJC, laboratory investigation of erythrocyte sedimentation rate/CRP levels, and a PtGA or global assessment on a VAS [30], thus covering similar elements as CDAI/SDAI. However, DAS-28 scores are calculated differently to those of CDAI/SDAI, with a total ranging from 0 to 9.4 [30].

Outcome variables included the number of patients in whom the measures were utilized; the mean [standard deviation (SD)] and median [interquartile range (IQR)] score of each disease measure; and the proportion of patients in remission, or with low, moderate, and high disease activity assessed according to RAPID3, CDAI, SDAI, and DAS-28 scores. Using RAPID3, remission was defined as a score ≤ 1.0, low disease activity as a score > 1.0–2.0, moderate disease activity as a score > 2.0–4.0, and high disease activity as a score > 4.0 [19, 30]. For the CDAI, a score of ≤ 2.8 was considered remission, > 2.8–10 low disease activity, > 10–22 moderate, or > 22 high activity. For SDAI, remission was scored ≤ 3.3, low disease activity > 3.3–11, moderate > 11–26, or high > 26 [20, 30]. DAS-28 scoring was interpreted as remission < 2.6, low disease activity 2.6– < 3.2, moderate disease activity 3.2–5.1, or high disease activity > 5.1 [30].

Patient demographics were collected at index, including age category, sex, race/ethnicity, and year of index date. Insurance type (as of June 2020) and comorbid RA diagnosis post-index by year were also recorded.

Sample Size and Power Considerations

Owing to the descriptive nature of this study, sample size and power calculations were not required; a feasibility assessment was conducted in 7000 patients with SLE (approximately 25% of patients with SLE in the UR NICE database). Of these patients, 6417 patients with ≥ 1 SLE diagnosis between 1 January 2010 and 31 December 2019 and ≥ 5 years of age at the date of the first diagnosis of SLE were eligible for inclusion. Among these patients, 1990 patients had ≥ 5 years of follow-up post-index.

Statistical Analysis

Baseline patient demographics were summarized, and rheumatology-specific characteristics were analyzed by year and cumulatively across the 5-year observation period (Years 1–5). Mean (SD) and median (IQR) scores were used to summarize continuous variables, and frequencies (proportions) were used to summarize categorical variables. No hypothesis testing was conducted, and thus no p values are available. If multiple measurements were taken for the same continuous measure during a given year or over the 5-year period, the mean of the values were calculated per patient.

Subgroup analyses were carried out based on race, insurance type as of June 2020, and disease activity based on RAPID3 score during follow-up categorized as either low (0–4, thereby including scores denoting remission, low disease activity, and moderate disease activity) or high (> 4).

RESULTS

Patient Disposition

Of the 30,037 patients with SLE identified from UR NICE electronic medical records, 10,870 (36.2%) were diagnosed with SLE between 1 January 2010 and 31 December 2014. Of these, 10,866 were ≥ 5 years of age at the index date. Only 157 (2.6%) patients were in the 5–19 years of age category. Overall, 5990 (55.1%) patients with SLE had ≥ 5 years of clinical activity following the index date and were included in the study.

Patient Demographics and Disease Characteristics

Most patients were between 20 and 64 years of age (n = 4994/5990, 83.4%), of White race (n = 2822/4062, 69.5%), and female (n = 5490/5981, 91.8%) (Table 1), and the majority had commercial insurance as of June 2020 (Table S2; n = 3815/5990, 63.7%). Only 870 (14.5%) patients with SLE had a comorbid diagnosis of RA during the 5 years of follow-up (Table 2). Neuropsychiatric conditions and lupus nephritis made up the majority of other medical conditions and comorbidities observed in the population, with cumulatively 14.5% and 9.7% of the cohort, respectively, being affected. Musculoskeletal conditions cumulatively affected 3.7% of patients (Table S3).

Use of RA Disease Measures for SLE

The most frequently used RA disease measures were the Pain Index, SJC, TJC, MD-HAQ, PtGA, RAPID3, and PGA (Fig. 2a). Among these, Pain Index was the most commonly used

Table 1 Demographics at index date[a] (N = 5990)

n **(%)**	***N*** **= 5990**
Age, years[b]	
5–19	157 (2.6)
20–39	1469 (24.5)
40–64	3525 (58.8)
Above 65	839 (14.0)
Sex	
Patients with known sex data	5981 (99.8)
Female	5490 (91.8)
Male	491 (8.2)
Race[c]	
Patients with known race data	4062 (67.8)
White	2822 (69.5)
African American	954 (23.5)
Asian	69 (1.7)
American Indian/Alaskan Native	9 (0.2)
Native Hawaiian/Other Pacific Islander	6 (0.1)
Other	160 (3.9)
Multiple	42 (1.0)
Ethnicity[c]	
Patients with known ethnicity	3806 (63.5)
Hispanic or Latino	166 (4.4)
Not Hispanic or Latino	3615 (95.0)
Other	25 (0.7)

UR NICE United Rheumatology Normalized Integrated Community Evidence

[a]Index date was defined as the date of the first diagnosis of SLE in the UR NICE database

[b]As patient age was only available as 5-year intervals, patient birth year was imputed using the lowest age value of their corresponding age range. December 31 was then used as a proxy for patient's birth month/day when calculating age at index date

[c]Multiple records may be reported for each patient. Therefore, the non-missing record closest to the index date was used in this analysis

Table 2 Comorbid RA[a] diagnosis post-index (N = 5990)

n (%)	*N* = 5990
Year 1	631 (10.5)
Year 2	562 (9.4)
Year 3	561 (9.4)
Year 4	545 (9.1)
Year 5	540 (9.0)
Cumulative Years 1–5	870 (14.5)

CM clinical modification, *ICD-9* International Classification of Diseases 9th Revision, *ICD-10* ICD 10th Revision, *RA* rheumatoid arthritis

[a]RA was identified using ICD-9-CM codes 714.0–714.3x and 714.81 and ICD-10-CM codes M05.x, M06.0x, M06.1, M06.2x, M06.3x, M06.8x, M06.9, and M08.x

(cumulative Years 1–5: 71.3%) followed by MD-HAQ (cumulative Years 1–5: 49.8%). SJC, TJC, and PtGA were each used in around 40% of patients cumulatively across Years 1–5, and cumulative use of PGA over this period was 23.9%. The cumulative use of RAPID3 over 5 years was 39.5%. The remaining RA disease measures—CDAI, DAS-28, and SDAI—were used less frequently (cumulative Years 1–5: 15.0%, 6.8%, and 6.5%, respectively) (Table S4). For all RA disease measures, the frequency of use increased from Year 1 to Year 5. In particular, for RAPID3, use increased from 8.6% (n = 517/5990) in Year 1 to 32.7% (n = 1959/5990) in Year 5 (Fig. 2a).

When analyzed by subgroups, RA disease measures (excluding CDAI, DAS-28, and SDAI) were used in a greater proportion of White patients with SLE (cumulative Years 1–5: 29.5–76.8%) compared with African American patients with SLE (cumulative Years 1–5: 20.2–63.7%) (Table S5). In addition, use of these measures was more common in patients with Medicare insurance (cumulative Years 1–5: 28.0–76.3%) versus those with commercial insurance (cumulative Years 1–5: 22.0–69.0%) (Table S6). Finally, RA disease measures

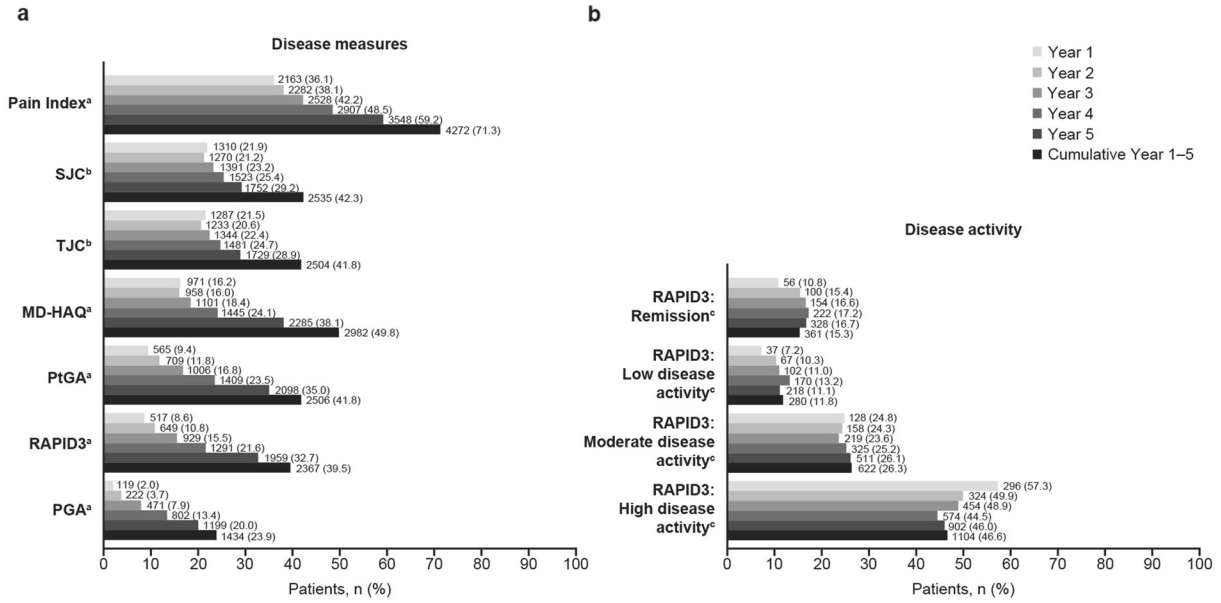

Fig. 2 Most frequently used RA disease measures (**a**) and disease activity level by RAPID3 (**b**) (N = 5990). [a]Scale: 0–10; [b]scale: 0–28; [c]RAPID3 cut-off values based on the literature; remission was defined as score ≤ 1, low disease activity as score > 1–2, moderate disease activity as score > 2–4, high disease activity as score > 4 [19]. *MD-HAQ* Multi-Dimensional Health Assessment Questionnaire, *PGA* Physician Global Assessment, *PtGA* Patient Global Assessment, *RA* rheumatoid arthritis, *RAPID3* Routine Assessment of Patient Index Data 3, *SJC* Swollen Joint Count, *TJC* Tender Joint Count

(excluding RAPID3 score) were used in a slightly greater proportion of patients with high SLE disease activity as measured by RAPID3 assessment (cumulative Years 1–5: 53.7–100.0%) compared with patients in remission or with low-to-moderate SLE disease activity (cumulative Years 1–5: 45.6–99.8%) (Table 3).

SLE Activity Using RA Disease Measures

Assessment scores remained relatively stable over the 5-year follow-up period for most measures, except for the MD-HAQ, for which scores slightly increased [mean (SD) score in Year 1: 1.5 (1.8), mean (SD) score in Year 5: 2.0 (1.9)] and PtGA and RAPID3, for which scores decreased [PtGA: mean (SD) score in Year 1: 4.9

Table 3 Use of RA disease measures by RAPID3 disease activity category

Disease activity category	Use of disease measure *n* (%)					
	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative Years 1–5
Low (N = 1263)						
Pain Index[a]	415 (32.9)	539 (42.7)	712 (56.4)	870 (68.9)	1123 (88.9)	1261 (99.8)
SJC	199 (15.8)	242 (19.2)	336 (26.6)	374 (29.6)	459 (36.3)	581 (46.0)
TJC	190 (15.0)	236 (18.7)	329 (26.0)	368 (29.1)	458 (36.3)	576 (45.6)
MD-HAQ[a]	196 (15.5)	291 (23.0)	464 (36.7)	695 (55.0)	1035 (81.9)	1218 (96.4)
PtGA[a]	214 (16.9)	319 (25.3)	495 (39.2)	735 (58.2)	1053 (83.4)	1221 (96.7)
RAPID3[c]	209 (16.5)	304 (24.1)	477 (37.8)	712 (56.4)	1059 (83.8)	1263 (100.0)
PGA[a]	45 (3.6)	105 (8.3)	235 (18.6)	391 (31.0)	574 (45.4)	673 (53.3)
High (N = 1104)						
Pain Index[a]	490 (44.4)	526 (47.6)	626 (56.7)	735 (66.6)	950 (86.1)	1104 (100.0)
SJC	309 (28.0)	321 (29.1)	382 (34.6)	456 (41.3)	531 (48.1)	640 (58.0)
TJC	298 (27.0)	304 (27.5)	359 (32.5)	432 (39.1)	519 (47.0)	633 (57.3)
MD-HAQ[a]	286 (25.9)	326 (29.5)	432 (39.1)	577 (52.3)	887 (80.3)	1074 (97.3)
PtGA[a]	319 (28.9)	354 (32.1)	467 (42.3)	610 (55.3)	873 (79.1)	1054 (95.5)
RAPID3[b]	308 (27.9)	345 (31.3)	452 (40.9)	579 (52.4)	900 (81.5)	1104 (100.0)
PGA[a]	46 (4.2)	79 (7.2)	182 (16.5)	346 (31.3)	511 (46.3)	593 (53.7)

"Low" includes RAPID3 scores of 0–4, thereby including patients in remission and those with low disease activity and moderate disease activity. "High" denotes RAPID3 scores of > 4

Follow-up period was defined as the period of time spanning from the date of the first diagnosis of SLE recorded in the UR NICE database (index date) to the end of observation (month 60/Year 5 of clinical activity)

MD-HAQ Multi-Dimensional Health Assessment Questionnaire, *PGA* Physician Global Assessment, *PtGA* Patient Global Assessment, *RA* rheumatoid arthritis, *RAPID3* Routine Assessment of Patient Index Data 3, *SJC* Swollen Joint Count, *TJC* Tender Joint Count, *UR NICE* United Rheumatology Normalized Integrated Community Evidence

[a]For patient Pain Index, increasing scores indicate greater pain levels. For MD-HAQ, increasing scores indicate worse functioning. For PGA and PtGA, increasing scores indicate higher level of disease activity

[b]RAPID3 cut-off values based on the literature; remission was defined as score ≤ 1, low disease activity as score > 1–2, moderate disease activity as score > 2–4, high disease activity as score > 4 [19]

(2.6), mean (SD) score in Year 5: 4.2 (2.7); RAPID3: mean (SD) score in Year 1: 4.3 (2.2), mean (SD) score in Year 5: 3.7 (2.3)] over the 5-year period. Of note, disease activity was consistently scored higher using PtGA versus PGA measures [cumulative Years 1–5 mean (SD) scores: 4.2 (2.6) versus 2.5 (2.3), respectively], and using Pain Index versus TJC and SJC measures [cumulative Years 1–5 mean (SD) scores: 4.2 (2.6) versus 3.1 (4.5) and 1.0 (2.4), respectively] (Fig. 3). Although scores generally decreased among patients evaluated with the SDAI and DAS-28 measures [SDAI: mean (SD) score in Year 1: 22.5 (14.7), mean (SD) score in Year 5: 13.3 (10.2); DAS-28: mean (SD) score in Year 1: 3.4 (1.7), mean (SD) score in Year 5: 2.8 (1.2)], relatively few patients were assessed using these measures (Table S4). Median (IQR) scores are also reported in Fig. 3 and Table S4.

The proportion of patients in remission or with low disease activity by RAPID3 increased over the 5-year period (Year 1: $n = 93/517$, 18.0%; Year 5: $n = 546/1959$, 27.9%; Fig. 2b). A similar trend was also observed for less frequently used RA disease measures (Table S4).

DISCUSSION

This real-world, retrospective, observational cohort study analyzed medical data from patients with SLE from a large US rheumatology electronic medical records database. The results indicate that the use of RA disease measures in monitoring patients with SLE in clinical practice in the USA is infrequent but has increased

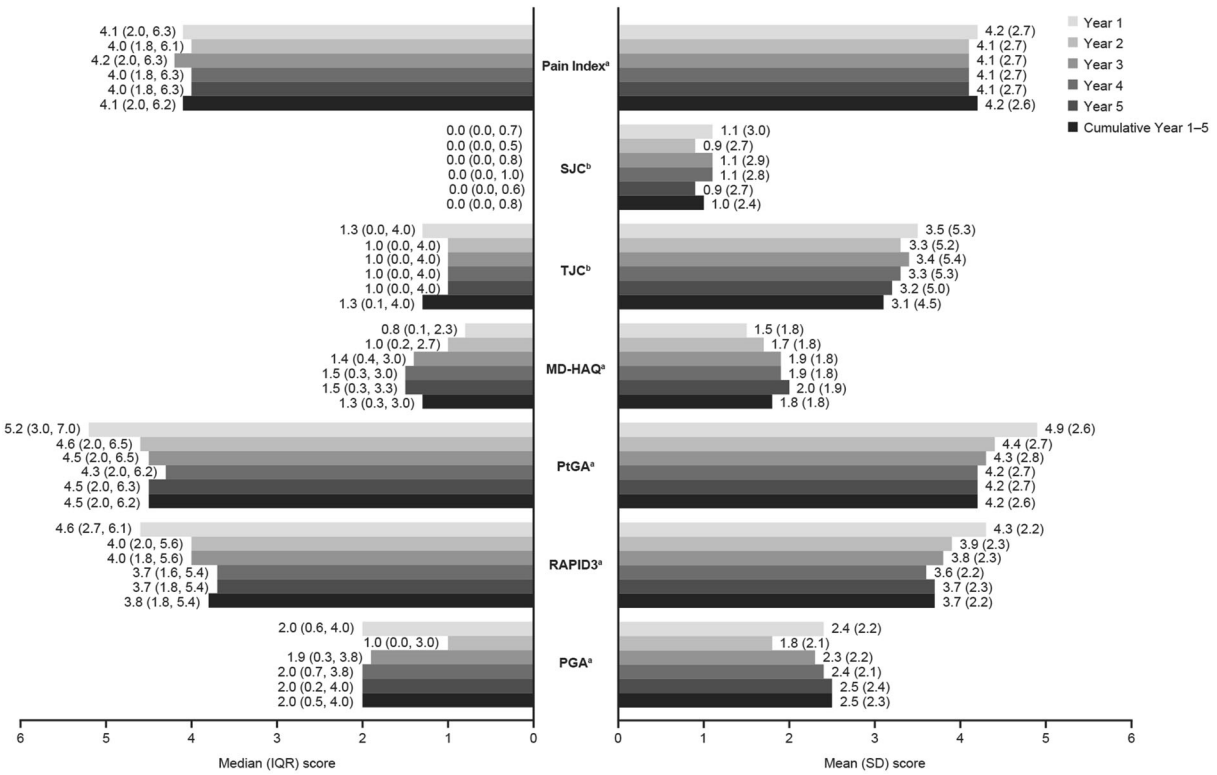

Fig. 3 Median and mean RA-specific disease measure scores over time. Higher scores indicate higher level of disease activity. [a]Scale: 0–10; [b]scale: 0–28. *IQR* interquartile range, *MD-HAQ* Multi-Dimensional Health Assessment Questionnaire, *PGA* Physician Global Assessment, *PtGA* Patient Global Assessment, *RA* rheumatoid arthritis, *RAPID3* Routine Assessment of Patient Index Data 3, *SD* standard deviation, *SJC* Swollen Joint Count, *TJC* Tender Joint Count

over time. It is worth noting that only 14.5% of patients with SLE in this cohort had a diagnosis of comorbid RA during the 5 years of follow-up, which suggests that the RA disease measures are being used to monitor SLE specifically, rather than for patients with overlapping symptoms or change in clinical impression, or in only those patients with SLE who present with comorbid RA. The 5-year follow-up period was chosen as a length of time that would allow any trends in the change of use of the RA disease measures to be noted. The most frequently used RA disease measures were Pain Index, SJC, TJC, MD-HAQ, PtGA, RAPID3, and PGA. Among these, Pain Index and MD-HAQ were the most commonly applied cumulatively across 5 years of follow-up (Pain Index: 71.3%; MD-HAQ: 49.8%). While the use of RAPID3 and PtGA was similar in this study, RAPID3 may have better utility in SLE as it is able to more rapidly provide information on the patient's quality of life [19].

The use of RA disease measures in patients with SLE increased year on year over the 5-year period studied. However, assessment scores remained relatively stable for most measures.

Use of the Pain Index, SJC, TJC, MD-HAQ, and PtGA was more common in patients with high disease activity, as scored by RAPID3, than in those with lower disease activity. This is likely because patients with higher disease activity experience more severe disease and damage accrual than patients with lower activity, which in turn may require more frequent assessment of disease activity and progression [31]. In addition, although no threshold values were applied to define high disease activity in Pain Index, SJC, TJC, MD-HAQ, PtGA, and PGA measures, disease activity was consistently scored higher (reflecting higher disease activity) using PtGA versus PGA measures. This may correspond to the discordance between Pain Index and TJC/SJC scores over the 5-year period, and be reflective of the known discordance of disease activity and impact of SLE on quality of life between physician (i.e., objective) and patient (i.e., subjective) assessments [10, 11].

Gathering updated information regarding disease activity is important in SLE; however, in everyday clinical practice physicians rarely use traditional, SLE-specific measures, such as SELENA-SLEDAI and BILAG, as they require laboratory testing, which can be difficult and time consuming [12, 13]. Moreover, these measures do not adequately capture patient-reported quality of life [10, 11]. The RAPID3 index, calculated from the sum of three 0–10 patient self-reported scores, takes only 5–10 s to complete and may be used in clinical practice as a simple and quick way to start physician–patient conversation about the activity/severity of SLE over time and provide insight into the patients' well-being [19, 32]. RAPID3, together with other RA disease measures when used alongside SLE-specific measures, may help to complete the picture of a patient's overall condition, by providing information on patient-reported health status. Furthermore, using these quick, easy-to-use RA disease measures in between SLE-specific measures has the potential to reduce the administrative burden associated with these traditional methods. It is interesting to note that, in clinical practice, while RA disease measures are applied to SLE, SLE disease measures are not applied to RA. This could be because RA disease measures focus on inflammatory markers and global physician/patient assessments, which are applicable to other autoimmune diseases [19–21, 23, 29], whereas SLE disease measures assess multiorgan involvement, which may not be applicable to RA [7].

The use of RAPID3 in isolation has been demonstrated to be inadequate to monitor disease activity in RA [33], and RAPID3 is recognized to communicate "patient distress" but not to differentiate between RA-related disease activity (e.g., synovitis) and symptoms arising from noninflammatory, comorbid conditions (e.g., fibromyalgia, depression, etc.) of relevance to SLE. Further, differentiating inflammatory and noninflammatory symptoms is critical to the optimal management of SLE [34]. Thus, RAPID3 results, as a subjective reflection of distress, would ideally be paired with an SLE-specific measure. The lack of evidence of widespread application of such an SLE-specific companion measure suggests that the available measures have either been rejected as infeasible for clinical use or that limited familiarity with them remains a barrier to adoption. In either

case, the identification of a clinically applicable SLE-specific measure remains critical to advancing patient care. Applying RA disease measures in conjunction with SLE-specific measures, such as SELENA-SLEDAI and BILAG, appears to be an interim solution to fill this need until a more direct SLE measure is developed, disseminated, and implemented.

To the best of our knowledge, this is the first study assessing the real-world use of RA measures to characterize SLE disease severity and burden. However, there are limitations to our study that affect the generalizability of the findings. These include the duration of follow-up for the medical history of patients; $\geq$ 5 years follow-up may not be representative of a patient's entire life course of disease. In addition, since an inclusion criterion was that patients were required to survive for $\geq$ 5 years post SLE diagnosis, the results may not be generalizable to patients with more severe disease who may die within 5 years of SLE diagnosis. Similarly, as the UR NICE database only includes patients seen in rheumatology clinical practices, the results may not be generalizable to all patients with SLE in the USA. Another limitation is that the study population included both incident and prevalent cases of SLE, as the date of first SLE diagnosis was not recorded for all patients (i.e., for patients first diagnosed outside of the UR NICE network). In addition, physician bias towards the use of RA disease measures may affect score stability over time. As the analyses were exploratory and descriptive in nature, no formal hypothesis testing was performed. Finally, the increased use of RA disease measures over the observation period may simply reflect their increased use in a community-based rheumatology practice in general, for all patients seen in outpatient clinics. Alternatively, the increased use could also be due to payer demands or increased emphasis on healthcare quality measures in general in the USA.

CONCLUSIONS

In summary, in this analysis of real-world rheumatology data from the USA, use of RA disease measures to assess patients with SLE was generally infrequent, but increased over time. The most frequently used measures were Pain Index, SJC, TJC, MD-HAQ, PtGA, RAPID3, and PGA. Determination of the rationale for the increased application of RA disease measures among patients with SLE over time requires further exploration; however, their use may provide an alternative approach for measuring disease activity and outcome, as well as improving care for patients with SLE.

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Disclosures. Christopher F. Bell and Bernard Rubin are employees of GSK and hold stocks and shares in the company. Shirley P. Huang is a former postdoctoral fellow at GSK and held stocks and shares in the company. Louise H. Yu, Maral DerSarkissian, Guillaume Germain, Yuqian M. Gu, and Mei Sheng Duh are employees of Analysis Group, which received research funding from GSK to conduct this study. Andrew L. Concoff is an employee of United Rheumatology, which is the source of the data for the present project. Carlyne M. Averell is a former employee of GSK and held stocks and shares in the company. Daniel J.

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Compliance with Ethical Guidelines. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. No direct patient contact or primary collection of individual human patient data took place. Study results omitted patient identification, therefore informed consent, ethics committee or institutional review board approval was not required.

Data Availability. The datasets generated and/or analyzed during the current study are not publicly available due to the proprietary nature of the electronic health records. The protocol and study report may be available from the corresponding author on reasonable request.

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