The Minimally Important Difference for Patient Reported Outcomes in Systemic Lupus Erythematosus Including the HAQ-DI, Pain, Fatigue, and SF-36

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ABSTRACT. ***Objective.*** We studied patients with systemic lupus erythematosus (SLE) in 1 clinical practice, and patients enrolled in the 1000 Canadian Faces of Lupus database, to determine the minimally important difference (MID) for pain, fatigue, sleep, Health Assessment Questionnaire-Disability Index (HAQ-DI), and Medical Outcomes Study Short Form-36 (SF-36) Physical Component Score (PCS) and SF-36 Mental Component Score (MCS) using a patient-reported overall health status anchor.

Methods. Patients with SLE who had 2 consecutive clinic visits and completed a HAQ-DI and a pain, fatigue, and sleep visual analog scale (VAS) (0-100), and an overall health status question: "How would you describe your overall status since your last visit?": much better, better, the same, worse, or much worse were included. Those who self-rated as better or worse were considered the "minimally changed" subgroups. Patients with 2 consecutive annual visits in the 1000 Canadian Faces of Lupus database who completed the SF-36 and health transition question were eligible.

Results. There were 202 patients in London, Ontario (94% women, mean age 50 yrs, mean disease duration 10 yrs). MID for better and worse on a VAS (0-100) were: pain (–15.8, 8.5), fatigue (–13.9, 9.1), and sleep problems (–8.6, 7.6). The MID for HAQ-DI (scale 0 to 3) was –0.08 (better) and 0.14 (worse). The MID for SF-36 was 2.1 (better) and –2.2 (worse) for the PCS and 2.4 (better) and –1.2 (worse) in the MCS.

Conclusion. The MID in patients with SLE may be different bidirectionally depending on the measured outcome. The mean change observed for those reporting better than worse outcome in pain and fatigue was greater for better versus worst, in contrast to the HAQ, where the mean change was greater for worsening. (First Release Sept 1 2009; J Rheumatol 2009;36:2231–7; doi:10.3899/jrheum.090193)

Key Indexing Terms:
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Systemic lupus erythematosus (SLE) is an autoimmune disease affecting approximately 1 in 1000 persons with a bias towards women between the ages of 20-50 years[1,2]. The American College of Rheumatology (ACR) includes 11 classification criteria, of which a patient must have at least 4 to be classified as having SLE[3]. SLE may be characterized by a combination of periods of remission or low disease activity and flares or periods of increased disease activity; this fluctuation in disease activity, in turn, has direct effect on quality of life. Since SLE is a chronic disease with no known cure, improving a patient's quality of life (QOL) and maintaining disease remission become important goals for the treating physician.

Patients are known to have poorer health related quality of life (HRQOL) regardless of the measurement tool[4]. Factors such as fatigue, pain, and sleep disturbances, as well as features of inflammation and damage and side effects from medications may influence QOL. Fatigue prevalence as high as 80% has been recorded in patients with SLE, and the prevalence of poor sleep is 60%[5]. Even though these complaints are not included as ACR classification criteria, they are very common and significantly affect patients' day to day functioning. Fatigue, pain, and poor sleep may be due to the disease itself, the psychological effects of having a chronic illness, comorbidities frequently associated with SLE (including fibromyalgia), or other patient specific factors. Because of this, it has been debated whether HRQOL

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factors actually correlate well with disease activity. As noted, fibromyalgia is common in patients with SLE; 25% of patients with SLE have concurrent fibromyalgia compared to 2-12% in the general population, which may greatly influence the HRQOL independent of the activity of the SLE[6,7].

QOL factors, such as good quality sleep, fluctuate so frequently that it can be difficult to determine how large a change is necessary for a patient to perceive improvement or worsening — the minimally important difference (MID). Determining the MID for fatigue, pain, and sleep quality in patients with SLE will help determine the effect a treatment has had on a patient in clinical trials and for clinicians to establish treatment recommendations for patients with SLE. For example, if a therapeutic agent had results much greater than the MID, and it worked within an individual, it would be reasonable to expect that the patient would perceive benefit from this agent.

There are several ways to determine the MID, one being an anchor approach, in which patient reported outcomes are anchored to a global assessment rating. Another approach is estimating the MID using a social comparison[8]. A recent study using this approach assessed MID of fatigue in patients with SLE by first having patients score their fatigue, then interview other patients with SLE, and finally compare their fatigue with the other patients. Seven fatigue instruments were used and the MID was calculated using 2 different methods. The MID of some patient reported outcomes have been determined in SLE, but usually not via serial assessments of patients in clinical practice as is done here.

Several instruments have been used to measure HRQOL in SLE. One widely used health assessment questionnaire is the Medical Outcomes Study Short Form (SF)-36, which consists of 36 questions relating to physical and mental health[9]. The answers are aggregated to calculate a physical component summary score (PCS) and mental component summary score (MCS). In rheumatoid arthritis (RA), MID for SF-36 PCS of 4.4 and MCS of 3.1 have been reported[10]. In SLE, the Canadian average for the PCS and MCS is 40.64 and 45.88, respectively[11]. The SF-36 is the most frequently used HRQOL measurement in patients with SLE and the questions relating to the physical health have significant correlations with the Systemic Lupus Activity Measure (SLAM) and SLE Disease Activity Index (SLEDAI), but some of the correlations are weak[4,12,13]. The Health Assessment Questionnaire-Disability Index (HAQ-DI) is a self-reported functional index that is widely used in RA[14]. It has been used less in SLE, as some patients with SLE do not have musculoskeletal complaints and many do not have inflammatory joint disease[15].

We hypothesized that the MID scores would be different bidirectionally (improving and worsening) and that MID scores could vary according to the disease activity.

MATERIALS AND METHODS

London, Ontario SLE cohort. Patients with SLE were studied at an outpatient rheumatology clinical practice in a hospital affiliated with the University of Western Ontario. Ethics approval was obtained from the Research Ethics Board at The University of Western Ontario. According to our ethics board, consent was not needed as the forms were all completed as part of our routine care, so the data were obtained by a thorough chart review. A HAQ consisting of questions regarding a patient's ability to perform activities of daily living is completed by each patient of the Rheumatology Clinic at every visit, to the best of the patient's ability, along with visual analog scales (VAS, 0-100 mm) for pain, fatigue, and quality of sleep, and a question asking about overall health status on a 5-point Likert scale. Patients were eligible for inclusion if: (1) they were diagnosed with SLE according to the ACR criteria[3]; (2) they were seen at 2 consecutive visits not more than 16 months apart; (3) their chart contained 2 completed HAQ, and VAS scores for pain, fatigue, and sleep problems done at these 2 consecutive visits; and (4) the overall health transition question had been completed (at least) at the second of the 2 visits.

The HAQ was scored and was not modified for assistive devices or categories requiring help from another person. The HAQ was considered usable if the patients completed a minimum of 6 of 8 categories and completed all VAS measuring pain, fatigue, and sleep problems, on a scale from 0 (none) to 100 mm (worst). The scores for pain, fatigue, sleep, and HAQ-DI were anchored to the 5-point overall health status question asking "How would you describe your overall status since your last visit? much better, better, the same, worse, much worse", to determine the MID. The HAQ MID was also calculated after stratifying by the presence of arthralgias or arthritis versus no problems with arthralgia/arthritis as determined by the arthritis question of the SLAM questionnaire[12]. Consistent scoring criteria were used for the VAS: if the patient's mark was between 2 millimeter points it was rounded up, a checkmark was scored where the point of the checkmark lined up, a line was scored where it crossed the scale, an X was scored where the lines intersected, and a circle's midpoint was recorded. The MID was determined as the change observed in the minimally changed groups ("better" or "worse"). The patients who reported that they were better (or worse) on the overall health status question were defined as the minimally changed subgroups. The changes in their pain, fatigue, sleep, and HAQ-DI for these groups were used to estimate the MID. This was compared to the change scores for the groups that were the same, much better, or much worse.

1000 Canadian Faces of Lupus Cohort. Each site that contributed data had ethics approval from their institutional ethics review boards and all patients signed consent to be enrolled in the 1000 Faces of Lupus study. In addition, the 1000 Canadian Faces of Lupus database was used to study the MID in the SF-36. The SF-36 consists of 36 questions that constitute a generic measure of physical and mental health; SF-36-2 is the second version of the form. The 1000 Canadian Faces of Lupus is a multicenter Canadian registry created to collect information on patients with SLE; at 14 sites 1722 patients have been enrolled to date. Patients meeting the ACR criteria for SLE[3] are seen annually to fill out background and demographic information, the SLE Activity Questionnaire (SLAQ)[16], and the SF-36-2[9]. The SLAQ is a patient completed questionnaire that measures possible disease activity. The investigating rheumatologist also completes annual forms regarding current disease activity and damage, the SLAM[12], the SLEDAI-2K[13], and the Systemic Lupus International Collaborating Clinics (SLICC) questionnaire[17]. The SLAM and SLEDAI measure clinical SLE disease activity and the SLICC measures disease damage. SLEDAI-2K is the SLEDAI 2000 version which is a modified version of SLEDAI and has high correlation to the original. Several sites did not have ethics approval for annual SF-36 or were not yet on schedule for their second year of followup and were thus excluded. Patients from 3 sites were eligible for inclusion if they had 2 consecutive annual visits within 16 months where the SF-36, SLAM, SLICC, and SLEDAI-2K were completed.

Data were extracted from the 1000 Canadian Faces of Lupus database

in Statistical Package for the Social Sciences (SPSS). The MID anchor for the SF-36 MCS and PCS was the overall health change question on a 5-point Likert scale of much better, somewhat better, the same, somewhat worse, and much worse, compared to the previous year, so the anchor for the 1000 Faces cohort annual visit was different than the single site clinic. In exploratory analyses, MID were stratified by disease activity (defined as above or below the baseline median score for SLAM and SLEDAI) and damage (above or below median SLICC).

Some patients were in both datasets and were included in each as the questions and time intervals were different (i.e., patients in 1000 Faces are seen annually and in addition are often seen in the hospital clinic every 6 months).

MID calculation. A change in patient reported outcomes should be related to the health transition question. Thus, a Spearman correlation coefficient > 0.30 between the outcome of interest and the health anchor is thought to be an appropriate correlation threshold[18]. The Spearman correlation coefficient is a measure of the strength of association between 2 variables. The Spearman correlation coefficient was calculated between the anchor question and each variable (pain, fatigue, sleep, HAQ, and SF-36 PCS and MCS) individually using SPSS. The MID was the amount of change in a measure compared to the health anchor of better or worse. The MID was calculated for each directional change (better and worse). Data were presented as (the most recent visit – previous visit), so that a change in pain, fatigue, sleep, or HAQ-DI that was negative was improvement; change in the SF-36 PCS or MCS that was negative was worsening. Using patients who were in both datasets, the MID for the HAQ-DI was also calculated in an exploratory analysis stratified by whether patients had ever reported arthralgia or arthritis, according to their 1000 Faces SLAM questionnaire, as HAQ has been widely used in other inflammatory arthritis such as RA. Not all patients with SLE have inflammatory arthritis, so we wanted to see if the HAQ MID would be different in those with or without inflammatory arthritis. Data were presented as mean and standard deviations (SD) and all p values were 2 tailed with significance at $p < 0.05$.

RESULTS

London, Ontario SLE Cohort. Two hundred eighty-four patients were identified in the initial screening; 78 were excluded for not having completed consecutive questionnaires within 16 months of each other and 4 did not meet the ACR criteria for SLE, leaving a final sample of 202 patients with SLE. The mean age (SD) was 50 (15) years and the mean (SD) disease duration was 10 (7.4) years; 194 (94%) were women (Table 1). The mean followup between visits was 7.5 months. Pain, fatigue, and sleep were scored on VAS of 0-100 mm. At baseline, 22 (11%) reported no pain and 4 (1.9%) reported maximum pain, 18 (9%) had no fatigue and 8 (4%) reported maximum fatigue, and 25 (12%) reported no sleep problems at baseline and 6 (3%) reported maximum sleep problems. The mean (SD) baseline scores were: 42.1 (29.9) for pain, 50.4 (30.6) for fatigue, 46.0 (30.6) for sleep, and 0.639 (0.610) for HAQ-DI. At followup they were, on average, not very different: pain was 39.0 (29.1), fatigue was 49.2 (31.4), sleep was 42.3 (32.4), and HAQ-DI was 0.644 (0.653). Among the 202 patients 14 (7%) reported being much better, 33 (16%) were better, 100 (50%) were the same, 50 (25%) were worse, and 5 (2%) were much worse.

The Spearman correlation coefficients for the overall health anchor question and change in outcomes were: pain 0.42, fatigue 0.33, sleep 0.28, and HAQ 0.29 ($p < 0.01$ for all). Table 2 shows the change scores for the outcomes pain, fatigue, sleep, and HAQ-DI. On average, patients who reported being better had a smaller change than much better, likewise with worse compared to much worse. The group that stayed the same had smaller mean incremental changes. The data appeared normally distributed. Except for the HAQ, on average there was more change needed to have a perception of improvement compared to worsening.

Table 1. Baseline and followup characteristics in the single site London, ON cohort of patients with systemic lupus erythematosus.

Characteristic	Baseline Mean (SD)	Followup Mean (SD)
Age, yrs	50 (14)	
Sex, % female	94	
Disease duration, yrs	10 (7.4)	
Visit time interval, mos	7.5 (3.4)	
Pain (0–100)*	42.1 (29.9)	39.0 (29.1)
Fatigue (0–100)*	50.4 (30.6)	49.2 (31.4)
Sleep (0–100)*	46.0 (30.6)	42.3 (32.4)
HAQ-DI (0–3)**	0.639 (0.610)	0.644 (0.653)

* 0 indicates no morbidity (no pain, no fatigue, no sleep disturbances) and 100 indicates severe morbidity. ** 0 indicates that activities of daily living are completed without any difficulty, an increasing score means increasing difficulty. SD: standard deviation; HAQ-DI: Health Assessment Questionnaire-Disability Index.

The MID for the HAQ-DI was also calculated separating patients who had reported arthralgia or arthritis, according to their 1000 Faces SLAM questionnaire (Table 3). Data were available for 126 patients at the single site study (London, ON) who also have data available in the 1000 Faces database. Numbers were small but no obvious differences were seen between the subsets of arthralgia/arthritis present versus absent.

1000 Canadian Faces of Lupus Cohort. Two hundred thirty-two patients from the 1000 Faces database who met inclusion criteria with 2 consecutive visits and complete data were included in the study, including 126 patients from our site in London, ON who are included in the MID calculations for pain, fatigue, sleep, and HAQ-DI. The mean age (SD) was 50 (14) years, with a disease duration of 10 (8.5) years; 210 (90%) were female (Table 4). The mean followup between visits was 12.1 months. The mean (SD) baseline scores for the SF-36 PCS and MCS were 37.0 (12.1) and 45.3 (12.2), and followup scores were 38.5 (12.1) and 47.0 (11.0). The Spearman correlation coefficients for the SF-36 PCS and MCS and overall health change anchor question were 0.30 and 0.22 ($p < 0.01$), respectively. The "same" group had a mean change similar to somewhat better for PCS and similar to somewhat worse for MCS. Table 5 shows the change scores for the SF-36 PCS and MCS in the 1000 Faces Cohort.

The MID for the SF-36 PCS and MCS were calculated

Table 2. Minimally important difference for the pain, fatigue, and sleep visual analog scale and Health Assessment Questionnaire-Disability Index (HAQ-DI) in the single site London, ON SLE Cohort (n = 202).

Patient-rated Overall Status	Pain Change Mean (SD) [95% CI]*	Fatigue Change Mean (SD) [95% CI]*	Sleep Change Mean (SD) [95% CI]*	HAQ-DI Change Mean (SD) [95% CI]**
Much Better	–18.7 (32.5) [–37.5 to 0.0]	–21.4 (30.6) [–39.1 to –3.8]	–25.4 (34.3) [–45.2 to –5.6]	–0.28 (0.43) [–0.52 to –0.03]
Better	–15.8 (16.0) [–21.5 to –10.1]	–13.9 (30.6) [–24.8 to –3.0]	–8.6 (24.6) [–17.3 to 0.1]	–0.08 (0.32) [–0.20 to 0.03]
The same	–3.7 (22.8) [–8.2 to 0.8]	–0.1 (28.3) [–5.7 to 5.5]	–5.5 (27.9) [–11.1 to 0.0]	–0.02 (0.29) [–0.08 to 0.04]
Worse	8.5 (21.5) [2.4 to 14.6]	9.1 (18.0) [4.0 to 14.2]	7.6 (24.6) [0.6 to 14.6]	0.14 (0.40) [0.03 to 0.26]
Much worse	20.8 (11.7) [6.3 to 35.3]	18.2 (38.1) [–29.1 to 65.5]	14.0 (12.9) [–2.1 to 30.1]	0.46 (0.69) [–0.40 to 1.31]

SD: standard deviation; CI: confidence interval. * Measured on a scale from 0–100 mm where 100 would indicate a worse outcome. The change is the score from the most recent visit minus the previous visit so that a negative score indicates an improvement in the outcome. ** The HAQ-DI is scored from 0–3, where 0 indicates no difficulty with activities of daily living (ADL). The HAQ-DI change score is that of the most recent visit minus the previous visit so that a negative score indicates less difficulty with ADL (an improvement).

Table 3. Minimally important difference for the Health Assessment Questionnaire-Disability Index (HAQ-DI) stratified by joint involvement in the single site London, ON SLE Cohort (n = 126).

Overall	Joint Involvement	Number of Patients	Mean HAQ-DI Change (SD)
Much better	No	2	–0.125 (0.177)
	Yes	6	–0.354 (0.374)
Better	No	5	–0.175 (0.244)
	Yes	16	–0.074 (0.360)
The same	No	9	–0.042 (0.272)
	Yes	52	–0.004 (0.312)
Worse	No	4	–0.062 (0.515)
	Yes	28	0.161 (0.422)
Much worse	No	0	NA
	Yes	4	0.580 (0.734)

* Patients were categorized as having joint involvement if they had ever reported a yes to the presence of arthralgias or arthritis in a 1000 Faces visit prior to or at the date of the baseline HAQ visit. SD: standard deviation.

Table 4. Baseline and followup characteristics in the 1000 Faces of Lupus cohort (n = 232).

Characteristic	Baseline Mean (SD)	Followup Mean (SD)
Age, yrs	50 (14.4)	
Sex, % female	90	
Disease duration, yrs	10 (8.5)	
Visit time interval, mos	12.1 (1.4)	
PCS, 0–100	37.0 (12.1)	38.5 (12.1)
MCS, 0–100	45.3 (12.2)	47.0 (11.0)
SLAM, n = 227	7.0 (4.2)	6.8 (3.8)
SLEDAI, n = 218	6.1 (4.7)	5.0 (4.4)
SLICC, n = 187	1.4 (1.7)	1.5 (1.7)

PCS: Physical Component Score; MCS: Mental Component Score; SD: standard deviation; SLAM: Systemic Lupus Activity Measure; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics.

with patients stratified by whether they were above or equal/below the baseline median SLAM score (6.0), SLEDAI score (6.0), and SLICC damage score (1.0). We found no difference in subsets of SLICC damage; there may have been more change needed to report much better in MCS and PCS for higher SLAM and SLEDAI, but the numbers were small (data not shown).

DISCUSSION

Determining the MID for patient reported outcomes in SLE is important in interpreting the results of clinical trials and in understanding how much change is relevant in clinical practice. A novel way of determining the MID is to ask large numbers of patients (being followed prospectively) to rate their overall health status (see answers to queries also), and then compare it to differences between visits for patient reported outcomes. This is novel because in many studies MID was calculated in treatment trials or comparing a patient reported change to changes in a physician assessment, a laboratory measure, or a disease related scale such as SLAM or SLEDAI. Other ways of determining a MID could be to ask patients if they think their fatigue or pain or function has changed from a previous visit or using different scales such as Likert scales with more than 5 points. However, we think a 5-point scale is sufficient as we published the MID in RA for HAQ-DI and pain and fatigue with the 5-point scale asking about change from last visit. The

Table 5. Minimally important difference for PCS and MCS from the SF-36 in the 1000 Faces of Lupus cohort (n = 232).

Patient-rated Overall Status	PCS Change Mean (SD)*	Change PCS 95% CI	MCS Change Mean (SD)*	Change MCS 95% CI
Much better, n = 21	8.4 (10.0)	3.8 to 12.9	9.1 (11.4)	4.0 to 14.3
Somewhat better, n = 54	2.1 (6.4)	0.4 to 3.8	2.4 (9.4)	–0.2 to 5.0
About the same, n = 99	2.0 (14.9)	0.5 to 3.4	1.2 (10.3)	–0.8 to 3.2
Somewhat worse, n = 52	–2.2 (6.9)	–4.1 to (–0.3)	–1.2 (10.6)	–4.1 to 1.8
Much worse, n = 6	–5.0 (9.5)	–15.0 to 5.1	0.7 (12.2)	–12.1 to 13.5

* The Physical and Mental Component Scores (PCS and MCS) are measured from 0–100, where 100 would represent perfect health compared to the rest of the population. * The change is the score at the most recent visit minus the previous visit; therefore a negative score indicates a worsening in the health of the patient.

MID for HAQ was actually less than what is reported in randomized controlled trials and thus the scale should be sensitive to detect MID[19,20].

The MID scores for improvement and worsening of pain were determined here for the first time in patients with SLE as a reduction of –15.8 for improvement and an increase of 8.5 for worsening. Interestingly, a much greater improvement in pain is needed before patients report feeling better compared to worse, as the confidence intervals (CI) do not overlap. It is important to note that CI overlapped for some changes and we considered the MID as the average change in each group of those who reported themselves as better or worse.

The MID scores for improvement and worsening of fatigue were –13.9 and 9.1. The MID for fatigue in patients with RA on the same scale in the same clinic was found to be –8.2 to –11.3 for improvement and 11.3 to 12.6 for worsening[20]. The estimates are similar, but perhaps in SLE it takes more change to perceive improvement than worsening, but this seems not to be the case in RA in clinical practice.

There is a larger correlation between the fatigue change and the health anchor question compared to the sleep change and the health anchor question (e.g., when the fatigue worsens the patient reports being "worse" on the health status question). This is not surprising, as sleep problems are very multidimensional and may not be related to SLE disease activity in many patients. The same could be said about fatigue, except that disease activity, with elevated inflammatory mediators, can certainly cause fatigue[21].

Our MID scores for improvement and worsening of the HAQ-DI were –0.08 and 0.14. These are remarkably close to the scores reported by our group in patients with RA in the same clinic, with HAQ-DI MID values of –0.09 and 0.15[19]. The direction of the MID is the same for SLE and RA for the HAQ, where a larger change is necessary before a patient reports feeling worse as opposed to better. We believe this is the first time the MID for the HAQ-DI in SLE has been determined. The HAQ may not be pertinent to a large proportion of patients with SLE, as some have no musculoskeletal problems and others may have problems with function as a direct consequence of internal organ involvement. However, the MID values are quite consistent with RA, and there were no marked differences in the HAQ MID estimates in the subsets with and without inflammatory joint disease.

Other MID have been determined in SLE for other features such as disease activity. A committee on SLE response criteria determined the MID by having patients fill out surveys and then physicians (blinded to the patient response) rated each patient with SLE as improved, worsened, or unchanged[22]. They defined the MID as the minimum change in the score that corresponded to a 70% agreement by their experts that the patient was improved or worsened using the SLAM and SLEDAI. The patients consisted of 2 cohorts from 2 different continents, and physicians from around the world. Their anchors were different as they compared individual patients' views to physicians'. As discussed by those authors, patients may answer questions based on their most dominant symptom (not necessarily their most serious), by their priorities, or by their severity at baseline. For instance, patients may rank their health status as poor due to their fatigue and arthralgia, while a physician may rate their disease activity as low if serious pathology (such as renal disease) is absent. This study also included their extreme groups, "much better" and "much worse," with the "better" and "worse" groups, which can affect the MID significantly.

In addition to that study[22], other groups have determined the MID for various HRQOL factors and disease activity using other measurement tools. Table 6 gives the MID of many scales used in SLE obtained from the literature. The only literature MID that overlap with our study are for fatigue. When normalized to the same scale used here (0–100), the MID values are similar except that they are reversed for better and worse (they find a value in the 10–20 range for worse and in the 2–10 range for better).

There are several limitations to determining the MID. Each method of calculating the MID produces a different value and the value depends on the original scale used[23]. This can make it difficult to settle on a value. Also, MID in trials may be different from clinical practice as a patient in

Table 6. Minimally important difference (MID) values for systemic lupus erythematosus (SLE) in the literature.

Instrument	Outcome	Scale	MID (worse, better)
FSS[8]	Fatigue	1–7 (positive)*	19.7, –1.4**
FSS[8]	Fatigue		9.7**
VT[8]	Fatigue	0–100 (negative)*	18.3, –7.3**
VT[8]	Fatigue		10.7**
MAF[8]	Fatigue	1–50 (positive)	18.2, –2.9**
MAF[8]	Fatigue		11.5**
MFI[8]	Fatigue	20–100 (positive)	16, –12**
MFI[8]	Fatigue		14.3**
FACIT-F[8]	Fatigue	0–52 (negative)	17.5, –5.3**
FACIT-F[8]	Fatigue		11.3**
CFS[8]	Fatigue	0–33 (positive)	9.7, –2.1**
CFS[8]	Fatigue		7.0**
Global RS[8]	Fatigue	0–100 (positive)	14.8, –2.9**
Global RS[8]	Fatigue		12.9**
SLEQOL[24]	Quality of life	40–280 (positive)	24.76
BILAG[22]	Lupus disease activity	(positive)	8, 7
SLEDAI[22]	Lupus disease activity	0–105 (positive)	8, 6
SLAM-R[22]	Lupus disease activity	0–84 (positive)	6, 4
ECLAM[22]	Lupus disease activity	1–17.5 (positive)	4, 3
SELENA-SLEDAI[22]	Lupus disease activity	0–105 (positive	8, 7
RIFLE[22]	Lupus disease activity		3, 4

* Positive means increasing severity with increasing score, negative means decreasing severity with increasing score. ** The mean scores were normalized to a 0–100 scale prior to the MID calculation. FSS: Fatigue Severity Scale; VT: Vitality Scale of SF-36; MAF: Multidimensional Assessment of Fatigue; MFI: Multidimensional Fatigue Inventory; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue Scale; CFS: Chalder Fatigue Scale; Global RS: Global Rating Scale with various wordings; SLEQOL: Systemic Lupus Erythematosus-specific Quality of Life Instrument; BILAG: British Isles Lupus Assessment Group; SLEDAI: SLE Disease Activity Index; SLAM-R: revised SLE Activity Measure; ECLAM: European Consensus Lupus Activity Measure; SELENA: Safety of Estrogen in Lupus Erythematosus: National Assessment; RIFLE: Responder Index for Lupus Erythematosus, response index.

a trial usually has active disease as part of the inclusion criteria. The change in a patient reported outcome score also depends on the patient's initial baseline status, where patients with worse baseline scores require greater improvement before it is relevant to them, and patients on the extremes cannot change much in 1 direction (floor and ceiling effects).

The overall health status question may not be as reliable an anchor as an objective assessment tool because of noise from comorbidities. The SF-36 anchor also does not refer specifically to health "related to SLE." Even if the anchor question asked about SLE related health, patients may not be able to discriminate which problems are attributable to SLE. This may be the case in SLE patients with fibromyalgia where the SLE can be inactive, but the fibromyalgia may cause a perceived poor health state. In addition, none of the outcomes we explored (pain, fatigue, poor sleep, HAQ-DI) is specific to SLE and the SF-36 questions inquire about many symptoms that are not relevant to patients with SLE. We did not look at the MID of SLE scores for this paper such as SLAM and SLEDAI.

A change anchor is also subject to recall bias, and the time frame may differ among questionnaires. For example, the HAQ-DI asks for answers based on the past week, whereas the SF-36 is for over the past month. However, our results for SLE are consistent with previous findings for SF-36 in RA, and fatigue in SLE on a 100 mm VAS (10,8).

Although our data were similar to results from other described methodologies and our sample sizes were large, our study has other potential limitations. The scores for the VAS and HAQ-DI were from a single rheumatologist's patients. This could present a problem when transferring the results to a clinical trial as the trial population may have different characteristics. A previous study has shown that in patients with RA the MID for the HAQ-DI was smaller in clinical practice patients than in trial patients[19]. Disease duration in this study was long; and patients with new onset SLE may have different baseline scores and thus their MID may be different. The effect of disease duration on HRQOL issues has not been established for SLE. Missing data could bias the results, since these patients may share characteristics such as illiteracy or severe disease that could make filling out numerous forms problematic; however, very few patients had incomplete data from the single site part of the study.

The pain, fatigue, sleep, HAQ, and SF-36 are patient

reported outcomes that were assessed in our study. We had a normal distribution of changed data and the scales had wide ranges of reported answers, which yielded a heterogeneous group allowing us to calculate the MID with certainty for better and worse in 2 large SLE groups. In addition, many outcomes have bidirectional MID, meaning that it may take a different amount to perceive being better than being worse. Understanding the MID results may help clinicians who treat SLE determine when a patient has perceived relevant change in patient reported outcomes, and should further research in interpreting results of clinical trials.

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