Systemic Lupus Erythematosus Disease Activity Index
Responder Index-50
(SRI-50)
SRI-50 Manual

Zahi Touma, Dafna D Gladman, Anne Mackinnon, Murray B Urowitz

University of Toronto Lupus Clinic
Centre for Prognosis Studies in the Rheumatic Diseases

Address: University of Toronto Lupus Clinic
Toronto Western Hospital
399 Bathurst Street 1E-410B,
Toronto, Ontario, Canada,
M5T 2S8

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Appendix 1  SLEDAI-2K Responder Index 50 (SRI-50) – Definitions
Appendix 2  Data retrieval sheet of SLEDAI-2K Responder Index-50 (SRI-50)
1. Introduction

SRI-50 is a Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Responder Index that can describe partial improvement, ≥50%, in disease activity between visits in lupus patients (1-2). As in the original SLEDAI, SRI-50 is based on the presence of 24 features in 9 organ systems and measures disease activity in SLE patients in the previous 30 days (3-6).

SRI-50 was developed to overcome the deficiency of the SLEDAI in its ability to measure partial response (1,2,7,8). SLEDAI was developed as a global disease activity index and evaluates items as present or absent in the past 30 days (3-6). Thus SLEDAI utility in clinical trials is limited as it cannot reflect partial improvement in a disease manifestation.

2. SRI-50

We used SLEDAI-2K to build the new responder index, SRI-50. A minimum of 50% improvement was felt by clinicians to reflect a clinically significant improvement.
2.1 SRI-50 definitions
The SRI-50 Definitions constitute a 2-page document (Appendix 1) detailing definitions for the 24 descriptors of the SRI-50 to define ≥50% improvement. Each descriptor refers to the 30 days preceding the assessment date. Rules for ascertainment were provided for each of the descriptors, be they physical findings, laboratory findings, patient self evaluation, health professional clinical assessment, laboratory results or diagnostic tools. The assigned scores for the descriptors of SRI-50 were derived by dividing the score of the corresponding SLEDAI-2K descriptor by 2.

2.2 SRI-50 data retrieval form
SRI-50 data retrieval form is a 2 page-document (Appendix 2). The SRI-50 data retrieval form was developed to standardize the recording of SLEDAI-2K descriptors in an efficient way to allow the calculation of SRI-50 scores.

2.3 Recording and scoring
Administration
SRI-50 data retrieval form is completed by the physician during the visit based on the history and clinical and laboratory findings. A complete history and physical examination are required in addition to the laboratory results related to the Index. Similar to SLEDAI-2K, for most patients it takes a couple of minutes to complete the form and the score is immediately known.
How the SRI-50 works

For the individual descriptors separate approaches are utilized by both physician and patient to evaluate the improvement between visits. The physician analyzes the results of physical findings, laboratory and diagnostic results (radiological, electrocardiogram and others) all based on hard well defined outcomes to complete the SRI-50 data retrieval form. For the descriptors which are more subjective and require patient self-evaluation (namely cranial nerve disorder, headache, the pain of pleurisy and pericarditis, and diffuse alopecia), the SRI-50 data retrieval form records the patient self evaluation based on numerical scale ranging from 1 to 10 (1 is mild and 10 is most severe). The physician collects the information from the patient and records it on the SRI-50 data retrieval form. For the descriptors related to neuro-lupus and more specifically psychosis and organic brain, we left the decision to the rheumatologist to determine if there is ≥50% improvement or not. Presumably the rheumatologist will confer/consult with other healthcare providers with expertise in this area e.g. neuropsychologists or psychiatrists to help him make the judgment of percentage improvement. In trials looking specifically at these outcomes such expertise could be included in the design. As an example in a trial of therapy for the treatment of acute cognitive dysfunction, evaluation by a neurocognitive expert will be included. Each descriptor refers to 30 days preceding the date of assessment as in the SLEDAI-2K 30 days.
**Scoring**

The method of scoring is simple, cumulative and intuitive as in SLEDAI-2K. In general if required one session of training is enough to become familiar with the scoring method of SRI-50.


One of three situations can occur when a descriptor is present at the initial visit:

1) the descriptor has achieved complete remission at follow up; in which case the score would be „0”; 2) the descriptor has not achieved a minimum of 50% improvement at follow up; in which case the score would be identical to its corresponding SLEDAI-2K value; or 3) the descriptor has improved by ≥ 50% (according to the SRI-50 definition) but has not achieved complete remission; in which case the score is evaluated as ½ of the score that would be assigned for SLEDAI-2K.

If a descriptor was not present at the initial visit, the value for SRI-50 at the follow up visit will be the same as that for SLEDAI-2K. This process is repeated for each of the 24 descriptors. Finally the SRI-50 score at follow up is evaluated as the sum of the 24 individual descriptors" scores.

SRI-50 score is evaluated at the follow up visit and corresponds to the sum of each of the 24 descriptors" scores found on the SRI-50 data retrieval form.

As recommended by the FDA in clinical trials, landmark analyses are important comparing the current patients” scores with those recorded at their baseline visit. These landmark comparisons can be made at a series of intervals e.g. at 2, 4,
and 6 months (compared to anchor visit) even though the primary outcome may be 6 months. Any deterioration in SRI-50 at 2 or 4 months would indicate a worsening in the original disease manifestation or the development of a new disease manifestation. Such occurrences could be secondary outcomes. In clinical practice, the physician is interested in how the patient is today compared to the last visit and here the comparison to the last visit may be appropriate.

3. SRI-50 Training and Certification

3.1 Training
The goal of the training and qualification process is to standardize administration and recording of the SRI-50 across study centers. Training in the correct use of the SRI-50 can be provided to each site prior to study start through dedicated sessions during the investigator meetings as well as online materials www.sri-50.com.

3.2 Certification
For certification, investigators will need to complete online training and examination modules. This includes case history examination, demonstrating the ability to correctly record and score baseline and follow-up visits and generate SLEDAI-2K and SRI-50 scores from a provided case history. Certification is required before administration of any SRI-50 assessments in clinical trials. Certification will be granted from the University of Toronto Lupus Clinic at the following link: www.sri-50.com after the investigator successfully completes the training (2 cases) and examination modules (5 cases).
4. Reliability

The reliability of SRI-50 was demonstrated in a multicenter, cross-sectional study with raters from Canada, United Kingdom and Argentina. This study was conducted on profiles derived from “real” adult patients receiving follow-up care at the University of Toronto Lupus Clinic. Ten rheumatologists (4 from university hospitals, 2 from community hospitals and 4 were postdoctoral rheumatology fellows) participated in this study. The level of training among clinicians in the use of the SRI-50 differed and 2 were untrained. The sampling strategy used assured that each of the 24 descriptors of SRI-50 was represented in at least 1 patient profile. The rheumatologists assessed the patients’ disease activity using the SRI-50 standardized data collection form. Rheumatologists derived SLEDAI-2K scores at the baseline visit and SRI-50 scores on follow-up visit, for the same patients on two occasions two weeks apart. The inter-rater/intra-rater intraclass correlation coefficient (ICC) (2,1) for SLEDAI-2K and SRI-50 were 0.99/0.99 and 0.98/0.98 respectively (7).

The SRI-50 is a reliable comprehensive tool to assess improvement in SLE disease activity. The use of a well-standardized form is essential to ensure the optimal performance of SRI-50. SRI-50 can be successfully used by both rheumatologists and trainees. Moreover SRI-50 performs equally in trained as well as untrained clinicians.
5. Validity of SRI-50

The initial construct validation of SRI-50 was demonstrated in a cross-sectional study on patients who had active lupus disease. SRI-50 was able to demonstrate partial improvement which would not have been discerned using SLEDAI-2K (1). In another study the concurrent construct validation of SRI-50 was evaluated (2). To determine the construct validity of SRI-50, all patients attending the Lupus Clinic from September 2009 to December 2009 were studied. Patients were assessed initially and on a follow-up visit according to both SLEDAI-2K and SRI-50 along with physician global assessment on a Likert scale which was considered the external construct. Of the 298 patients enrolled in this study 141 had a follow-up visit and were studied further. SRI-50 scores decreased more often in patients with Likert 6-7 (reflecting ≥50% improvement in disease activity) compared to Likert 5-4 (reflecting <50% improvement) with a decrease of ≥4. The decrease in SRI-50 scores were statistically and clinically more significant to the decrease in SLEDAI scores. SRI-50 was able to demonstrate partial improvement which would not have been discerned using SLEDAI-2K.
References


SLE Disease Activity Index Responder Index (SRI-50)