The systemic lupus activity measure-revised, the Mexican systemic lupus erythematosus disease activity index (SLEDAI), and a modified SLEDAI-2K are adequate instruments to measure disease activity in systemic lupus erythematosus


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Instruments to assess disease activity in systemic lupus erythematosus (SLE) were examined. Such instruments were the Systemic Lupus Activity Measure-Revised (SLAM-R), the Mexican version of the Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI) and the Modified SLEDAI-2000 (Modified SLEDAI-2K).

Type of intervention
Other: Disease activity assessment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a multi-ethnic US population with SLE.

Setting
The setting was secondary care (rheumatology clinics). The economic study was carried out in Alabama, Texas and Puerto Rico, USA.

Dates to which data relate
The effectiveness and resource use evidence was gathered between August 2002 and June 2003. The dates to which the prices referred were not reported, but were presumably contemporaneous.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing appears to have been carried out prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Patients with SLE were recruited, either when hospitalised due to a lupus flare, during a regularly scheduled follow-up clinic visit, or during a study visit while participating in a clinical trial. All patients satisfied four or more of the American College of Rheumatology (ACR) criteria for SLE. Ninety-two SLE patients were recruited, 32 in Alabama, 26 in Texas and 34 in Puerto Rico. Seven evaluations were completed in hospitalised patients, 43 during routine clinic
visits and 42 during clinical trial visits. No description was given of those patients who were excluded or refused to participate. Eighty-eight per cent of the patients were female. Forty-five per cent were Hispanics, 30% African Americans, 21% Caucasians and 4% Asians. The mean age was 39.2 (standard deviation, SD=11.8) years. The patients had established disease with a mean duration of 69.4 (SD=68.4) months.

**Study design**
This was a multi-centred, within-group comparison study (3 centres were included) with no follow-up of the patients. Each patient had a face-to-face interview and a physical examination with one of the study physicians. The physician administered all four of the study instruments to the patients. Laboratory tests were performed on the same day in all patients who were not hospitalised, and within a few days of the interview or examination for those who were hospitalised.

**Analysis of effectiveness**
The effectiveness outcomes assessed were:

- convergent validity,
- construct validity,
- levels of agreement between the instruments, and
- accuracy, that is, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy.

Convergent validity was assessed by comparing the total score of the three instruments using the Spearman rank correlation test. The physician's global assessment (PGA) of disease activity, assessed on a 10-cm anchored visual analogue scale (VAS) was used as a measure of construct validity. Bland-Altman plots were used to assess the level of agreement between the indices. The SLEDAI-2K was considered the 'gold' standard in assessing the sensitivity, specificity and discriminant validity of the other instruments. The PGA was also used as a 'gold' standard for further effectiveness comparisons.

**Effectiveness results**
In terms of convergent validity, the Spearman correlation coefficients were:

- 0.566, 0.595 and 0.555 between the SLAM-R and the MEX-SLEDAI, SLEDAI-2K and Modified SLEDAI-2K, respectively, (p<0.0001 for all comparisons);
- 0.804 and 0.755 between the MEX-SLEDAI and the Modified SLEDAI-2K and SLEDAI-2K, respectively, (p<0.0001 for all comparisons); and
- 0.924 between the Modified SLEDAI-2K and the SLEDAI-2K, (p<0.0001 for all comparisons).

In terms of construct validity, the correlation coefficients between the SLAM-R, MEX-SLEDAI, Modified SLEDAI-2K and SLEDAIA-2K, with the PGA, were 0.650, 0.540, 0.634 and 0.677, respectively, (p<0.0001 for all comparisons).

In terms of agreement between the instruments, there was better agreement between the Modified SLEDAI-2K and SLEDAI-2K, followed by the MEX-SLEDAI and SLAM-R. Agreement diminished as the scores increased (i.e. at higher level of disease severity).

In terms of discriminant validity, the Modified SLEDAI-2K had the best metric properties with an overall accuracy of 91%, a sensitivity of 76%, a specificity of 100%, a PPV of 100% and an NPV of 88%. The MEX-SLEDAI had an overall accuracy of 84%, a sensitivity of 58%, a specificity of 93%, a PPV of 84% and an NPV of 79%. The SLAM-R
had an overall accuracy of 66%, a sensitivity of 73%, a specificity of 63%, a PPV of 52% and an NPV of 80%.

Clinical conclusions
The authors stated that the SLAM-R, MEX-SLEDAI and Modified SLEDAI-2K have adequate convergent validity, acceptable construct validity and a high level of agreement, (though declining at higher levels of disease activity). When using the SLEDAI-2K as the 'gold' standard, the Modified SLEDAI-2K had the best metric properties, with the MEX-SLEDAI also proving satisfactory, while the SLAM-R did not perform as well in distinguishing patients with active and non-active disease. With the PGA as the 'gold' standard, comparable results were obtained.

Measure of benefits used in the economic analysis
No summary measure of health benefits was included. Therefore, a cost-consequences analysis was presented.

Direct costs
The costs considered in the economic analysis were those of the hospital (which appear to have been equivalent to those of the health care provider). The resources used were measured during the efficacy study, but the quantities and the costs were not reported separately. The authors included the cost of physician time for an interview and examination (an outpatient visit common to all alternatives) and the costs of laboratory tests (different among alternatives). The cost data were collected from one of the centres considered in the effectiveness analysis. It was not stated whether costs or charges were used, and the source of the prices and the price year were not reported. Discounting was not applied, but would not have not been relevant.

Statistical analysis of costs
No statistical analysis of the costs was included.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Not relevant since a cost-consequence analysis was undertaken. See the 'Effectiveness Results' section.

Cost results
The total cost of administering each questionnaire was $178 with SLAM-R, $172 with MEX-SLEDAI, $164 with Modified SLEDAI-2K and $216 with SLEDAI-2K.

The least expensive instrument was the Modified SLEDAI-2K (24% less costly than the SLEDAI-2K).

When only laboratory costs were considered (the cost of an outpatient visit in any event was constant across alternatives and equal to $146), the Modified SLEDAI-2K was 73% less costly than the SLEDAI-2K, whereas the MEX-SLEDAI and SLAM-R were 62% and 53% less costly, respectively, than the SLEDAI-2K.
Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
The Systemic Lupus Activity Measure-Revised (SLAM-R), the Mexican version of the Systemic Lupus Erythematosus Disease Activity Index (MEX-SLEDAI) and the Modified SLEDAI-2000 (Modified SLEDAI-2K) are reasonable alternatives to the SLEDAI-2K instrument for the assessment of disease activity in patients with systemic lupus erythematosus (SLE) around the world in either clinical or research settings. The Modified SLEDAI-2K showed better metric properties at lower cost and may be the best option of all.

CRD COMMENTARY - Selection of comparators
The choice of the SLEDAI-2K as a 'gold' standard comparator was not explicitly justified, given that the authors mentioned the large range of instruments available. You should decide whether the SLEDAI-2K is a widely used instrument in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a within-group comparison study, which appears to have been appropriate for the study question. It was unclear whether the study sample was representative of the study population, though study sample demographics and disease characteristics were provided, which would enable comparison with those of the population (i.e. multi-ethnic US patients with SLE). Appropriate statistical analyses were undertaken. However, each instrument was applied once and by one physician only to each patient. Therefore, the authors could not determine the inter- and intra-observer reliability or discriminant validity over time (sensitivity to change). The authors mentioned that physicians had received training in the use of each instrument, but neither the type of training received nor the usual instrument used in clinical practice were described. Scores were not tested for systematic differences aligned to patient characteristics such as race and gender.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
A cost perspective was not reported. It would appear that the costs were estimated from a hospital perspective, which seemed equivalent to a health care provider perspective. All the costs relevant to this perspective appear to have been included in the analysis. The authors also reported the results when the cost of the outpatient visits was excluded from the analysis, as this was common to all alternatives. The costs and the quantities were not reported separately, and it was unclear whether the laboratory costs reported were the mean costs per patient. These issues would hinder reflation exercises in other settings. Cost-differences among centres do not appear to have been investigated. It would have been useful in relation to generalisability to have had more detailed costs and quantities reported. As it is, the cost results may not be safely applied to other settings. No statistical analysis of the quantities or prices was performed. Charges might have been used to proxy costs. The date to which the prices referred was not reported.

Other issues
The authors made appropriate comparisons of their results with those from other studies and highlighted the additional information added by their study. They did not present their results selectively. The authors generalised their conclusions from a study sample of mainly female patients with a specific ethnic mix, drawn from the lower geographical regions of the USA, to all SLE patients worldwide, although no justification supporting this statement was provided. The authors believed that instruments which do not include immunologic laboratory tests (all but the SLEDAI-2K) do not suffer from a reduction in validity. However, their justification for this belief was that the value of the tests is "controversial", and that performing the tests may not be feasible in places which are "technologically
limited”. This does not appear to be an adequate scientific or health economic basis for discounting the use of these tests. The authors' judgement about the relative effectiveness of the instruments is thus open to criticism. In the absence of a true cost-effectiveness analysis, it becomes a subjective judgement whether the lower costs of the three instruments adequately compensates for the reduced level of information arising from the absence of immunologic laboratory tests. The authors acknowledged limitations to their study in terms of the lack of data showing adequate sensitivity to change in the studied instruments.

**Implications of the study**
The authors noted that the three instruments were considerably less expensive than the SLEDAI-2K, largely due to the cost of immunologic laboratory tests. They believed that excluding these tests does not limit the validity of the other instruments. They advised that the usefulness and feasibility of immunologic tests should be considered when choosing an instrument to assess disease activity, particularly when dealing with disadvantaged populations (presumably relating to less sophisticated or more poorly funded health care systems).

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