Patient-reported outcome measures in systemic lupus erythematosus by a web-based application:
A randomised, crossover, agreement study

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ABSTRACT

Objectives

Patient-reported outcome measures (PROMs) are evaluated in randomized controlled trials (RCTs) in patients with systemic lupus erythematosus (SLE), but not widely used in clinical practise. However, interest in incorporating PROMs into the management of SLE are increasing as PROMs provide a unique insight in the patient's perception of lupus disease activity. The objective was to assess agreement in PROMs answered using a web app vs an outpatient touchscreen among patients with SLE.

Methods

In a crossover, RCT, SLE patients answered the following PROMs in a random order using the web app and the outpatient touchscreen: Systemic Lupus Erythematosus Activity Questionnaire (SLAQ) Global Health, SLAQ Symptom score, SLAQ Total score, SLAQ Worsening, Pain Visual Analog Scale (VAS), Fatigue VAS, Patient Global Health VAS, Health Assessment Questionnaire Disability Index (HAQ-DI), Patient Acceptable Symptom State (PASS) and an Anchoring Question. Equivalence between the two device types was demonstrated if the 95% confidence interval (95%CI) of the difference in PROM scores was within the prespecified equivalence margins. Agreement between the two device types was assessed using mixed linear models.

Results

Thirty-four patients with SLE were included. Equivalence was demonstrated between the two device types for SLAQ Global Health with a difference of -0.21, (95%CI: -0.65 to 0.23). Moreover, equivalence was also found for HAQ-DI, Pain Visual Analog Scale (VAS) and Fatigue VAS whereas only comparability within the limits of the Minimal Clinically Important Difference (MCID) was demonstrated for VAS Patient Global Health. Statistically comparability was demonstrated for SLAQ Total score, SLAQ

Worsening, PASS and Anchoring Question (no predefined MCID/equivalence margins available). However, a statistically significant difference between device types was observed for SLAQ Symptom score of -0.56, (95%CI: -1.10 to 0.01). The difference was, however, very small when considering the scale range of 0-24; thus, not judged to be of clinical relevance. Preference for the web app was very high (91.2%).

Conclusion

For the first time ever, equivalence and comparability between two electronic device types for various PROMs were demonstrated among patients with SLE. Implementation of the device is expected to improve management of SLE.

Trial registration: Clinicaltrials.gov, NCT04411407, https://clinicaltrials.gov/ct2/show/NCT04411407?cond=SLE&cntry=DK&city=Aalborg&draw=2&rank=1.

KEY WORDS

Systemic lupus erythematosus, patient-reported outcome measures, smartphone application, minimally clinically important difference, equivalence, crossover study

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by formation of autoantibodies and multisystem organ involvement with a wide range of specific and non-specific organ symptoms that vary with disease activity and among patients (1,2).

Patient-reported outcome measures (PROMs) are a pivotal tool to complement the physician's evaluation and more fully reflect the patient's perception of SLE symptoms. However, PROMs are mostly assessed in clinical trials and not frequently in clinical practice (3). Both disease specific and generic PROMs has been evaluated and used in randomised controlled trials (RCTs) in SLE. (4–7) Currently, there is no international consensus about which PROMs are most preferable or essential in the management of patients with SLE.

The Systemic Lupus Erythematosus Activity Questionnaire (SLAQ) (8) is one of the more frequently used PROMs in SLE as it captures the impact of global health and disease activity, both considered essential outcomes when assessing patients with SLE (9). The validated SLAQ questionnaire (8,10) consist of 4 separate domains:

- SLAQ Global Health: the patient's evaluation of lupus disease activity on a NRS scale from 0-10.
- SLAQ Symptom: the patient's report of presence of lupus specific symptoms, range 0-24.
- SLAQ Total: the patient's evaluation of severity of lupus disease activity by a weighted score of the 24 lupus specific symptoms, range 0-44.
- SLAQ Worsening: the patient's evaluation of the presence/severity of lupus flare on a transitional scale, 0 (no flare), 1 (mild flare), 2 (moderate flare) or 3 (severe flare).

As technology has evolved, the assessment of PROMs has progressed from data collection on paper forms to electronic data capturing with digital solutions (11). Thus,

the outpatient touchscreen used in Denmark has previously demonstrated agreement with paper forms among patients with various rheumatic diseases (12,13). Electronic PROM data capture has many advantages over paper-based forms as secondary data entry errors are avoided and more exact and complete data are captured with minimal administrative burden (11). Thus, assessment of electronic PROM data captured on an outpatient touchscreen has been implemented in the management of various diseases worldwide during the past decades. However in recent years, interest in electronic reporting of PROMs through web applications (apps) has increased. It allows patients to access and respond to PROMs on their own device at their convenience; thereby, possibly minimising recall bias (11) and allowing reporting symptoms of flare as they occur. In addition, home access with an app or website has the following advantages over an outpatient touchscreen: no queue, no hygiene problems, discrete and comfortable data entry without disturbances.

Previously, the Danish Rheumatology Database (DANBIO) app as well as a web-based from home solution have proven to be comparable to the outpatient touchscreen among Danish patients with inflammatory arthritis (14,15). However, to our knowledge PROM agreement between two electronic device types among patients with SLE has not yet been evaluated. Throughout this paper, comparability and agreement refers to absence of a clinically relevant difference between device types whereas equivalence refers to an insignificant difference between device types i.e. within the limits of half of the Minimal Clinically Important Difference (MCID). Thus, the objective of this trial was to explore if electronic registration of PROMs with SLAQ Global Health as a primary outcome measure through the DANBIO web app is comparable, or even equivalent, to the outpatient touchscreen among patients with SLE.

METHODS

Patient and public involvement

A patient research partner (PRP) acknowledged the purpose of this trial, refined and approved the trial patient information material and approved the trial protocol. However, the PRP was not involved in inclusion of participants nor in the conduct or analyses of the trial. Research personnel will disseminate trial results to participants after publication.

Study design and participants

This trial was designed as a randomised, within-participants, crossover, agreement trial conducted at Aalborg University Hospital, Denmark. Patients ≥ 18 years old diagnosed with SLE in accordance with the 2019 European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) SLE Classification Criteria or judged to have a define SLE diagnosis by the rheumatologist were eligible for participating. Furthermore, experience with the PROM questionnaires in DANBIO (≥ 1 previous assessment) was required. Exclusion criteria included language barrier (PROMs were only available in Danish) and device barriers (participants with no access to smartphones or tablets).

Procedures

Eligible patients diagnosed with SLE were enrolled by a screening telephone contact from research personnel; thereafter, written informed consent was obtained. Participants were randomised in 1:1 ratio to:

- *Group web app → touchscreen (WA → TS):* participants completed PROMs on the DANBIO web app and after a "washout period" the same PROMs were answered on the outpatient touchscreen.

- *Group touchscreen → web app (TS → WA):* participants completed PROMs on the outpatient touchscreen and after a "washout period" the same PROMs were answered on the DANBIO web app.

A "washout period" of one to two days between the two PROM completions was prespecified to minimise potential recall bias as a short time period (e.g. 5 minutes) increase the risk of a biased over-agreement. Furthermore, the prespecified "washout period" was judged to be short enough to ensure that no major change in disease activity would occur.

Participants accessed the PROM questionnaire on the outpatient touchscreen with their personal civil registration number as usual practice. To access the DANBIO web app, the participant had to log on with their personal identification number (NemID) on their own smartphone or tablet from home or wherever convenient.

Patient-reported outcome measures

The participants answered the following PROMs on the two device types:

- SLAQ Global Health: described previously, MCID calculated to ± 1.495 (as described in 'Power and sample size calculation'), equivalence margins: ±0.75.
- SLAQ Symptom: described previously, MCID and equivalence margins not defined.
- SLAQ Total: described previously, MCID and equivalence margins not defined.
- SLAQ Worsening: described previously, MCID and equivalence margins not defined.
- Pain Visual Analog Scale (VAS): the patient's evaluation of pain within the last week on a 100 mm horizontal scale, range 0-100. MCID: ± 10 (16), equivalence margins: ±5.
- Fatigue VAS: the patient's evaluation of fatigue within the last week on a 100 mm horizontal scale, range 0-100. MCID: ± 10 (16), equivalence margins: ±5.

- Patient Global Health VAS: the patient's evaluation of disease activity within the last week on a 100 mm horizontal scale, range 0-100. MCID: ± 10 (16), equivalence margins: ±5.
- Health Assessment Questionnaire Disability Index (HAQ-DI): the patient's evaluation of physical function, range 0-3. MCID: ± 0.22 (16), equivalence margins: ± 0.11.
- Patient Acceptable Symptom State (PASS): the patient's evaluation of whether the current symptom state is acceptable, answered with "yes" or "no". MCID and equivalence margins are not defined.
- Anchoring Question: the patient's evaluation of change in disease activity since last visit, range: -3 (much worse), -2 (worse), -1 (slightly worse), 0 (unchanged), 1 (slightly better), 2 (better), 3 (much better). MCID and equivalence margins are not defined.

Objectives and outcomes

The primary objective was to assess if electronic registration of SLAQ Global Health by patients with SLE using the DANBIO web app was comparable, or even equivalent, to the outpatient touchscreen.

Secondary outcomes were comparability assessment between the two device types for the following PROMs: SLAQ Symptom, SLAQ Total, SLAQ Worsening, Pain VAS, Fatigue VAS, Patient Global Health VAS, HAQ-DI, PASS and an Anchoring Question. Finally, device preference was assessed.

Collected variables

The DANBIO database and the electronic medical journal were assessed to obtain the following baseline characteristics: sex, age, diagnostic criteria, disease duration, current SLE treatment, antinuclear antibodies (ANA), anti-double stranded deoxyribonucleic acid (anti-dsDNA), C-reactive protein (CRP), most recent (mean 8.5 months) physician assessed Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score and Systemic Lupus International Collaborating Clinics (SLICC) damage index. Furthermore, the most recent report of the following PROMs was obtained from the DANBIO database as baseline characteristics: SLAQ scores, VAS scores, HAQ-DI, PASS and anchoring question. However, these data were also included in the statistical analysis of primary and secondary outcomes as the mixed linear model was adjusted for PROM-level at inclusion as described in the statistical analysis section below.

All study data were collected in a dedicated electronic case report form (e-CRF) in the Research Electronic Data Capture (REDCap) system hosted by the North Denmark Region (17,18).

Power and sample size calculation

The sample size calculation was performed in accordance with the recommendations in the Difference Elicitation in TriAls ($DELTA^2$) guideline (19). To our knowledge, no MCID for SLAQ Global Health is defined; however, in a recent paper *by Katz et al.* improvement/worsening in SLE disease activity on a scale from 0 (not active) to 10 (very active) was defined as ±1.5 points (6). We estimated a similar minimal important difference for SLAQ Global Health from 1000 random SLAQ Global Health bootstrap samples from 44 patients with SLE from Aalborg University Hospital. The estimated median standard deviation (SD) was 2.99 (range: 2.25-3.62); thus, the MCID for SLAQ Global Health was: 0.5×2.99 = 1.495. Equivalence was defined as half of the effect that is considered a clinically relevant reduction i.e. half of the MCID; therefore, the

equivalence margins for SLAQ Global Health was ±0.75 (i.e. 0.5×1.495). However, for the sample size calculation, the more conservative estimate of the SLAQ Global Health equivalence margins that only allows minimal variance between two interventions was used i.e. based on the minimum value of the SD range of 2.25. This approach yields a conservative SLAQ Global Health equivalence margin of ±0.56 (i.e. 0.5×2.25×0.5).
As specified in the Trial Protocol (**Supplementary Data S1**) and the Statistical Analysis Plan (SAP) (**Supplementary Data S2**), a two one-sided tests analysis for additive equivalence of paired means with bounds -0.56 and +0.56 for the mean difference in SLAQ Global Health with a common standard deviation of 3.0 SLAQ Global Health points and correlation 0.95 between measures (i.e. a high degree of anticipated correlation between the two device types), a sample size of 33 patients was required to obtain a power of 90%. Thus, it was decided to aim for inclusion of 34 patients in total i.e. 17 patients in each intervention group.

Randomisation: Allocation concealment and implementation

Senior biostatistician Robin Christensen, with no clinical involvement in the trial, made the computer-generated randomisation sequence in SAS PROC PLAN before the start of the inclusion period. The randomisation sequence used permuted blocks and an allocation ratio of 1:1 to distribute participants in one of the two intervention groups. Thereafter, the independent data manager Johanne Hovgaard Winther (JHW) entered the randomisation sequence into the dedicated e-CRF in REDCap.

Statistical analyses

Analyses of trial data were done in accordance with the prespecified SAP, the Consolidated Standards of Reporting Trials (CONSORT) statements (20,21) and the Enhancing the QuAlity and Transparency Of health Research (EQUATOR) network

recommendation (22). Baseline characteristics were summarised as number and percentages or mean and standard deviations or median and interquartile range.

Primary and secondary outcomes were analysed using the intent-to-treat (ITT) population i.e. all patients who were randomised and completed the first PROM registration independent of subsequent protocol violations. A mixed linear model with both fixed effects (first or second registration; device [web app or touchscreen]), and the interaction between them, as well as random effects factor (patient identification number) adjusted for the assessed PROM-level at inclusion was applied. If the 95%CI of the difference in PROMs between the two device types was within the prespecified equivalence margins, agreement was considered satisfied (23). Agreement between the two device types for the primary outcome SLAQ Global Health was demonstrated with a Bland-Altman plot (24). McNemar's (paired) test was used to evaluate agreement for the two device types for PASS and SLAQ worsening. Thus, ordinal scores for all PROMs collected with the two device types was compared without any tests for associations with other outcome measures i.e. an anchor-based approached was not applied.

Analyses were done applying STATA (version 16) and SAS studio software (version 9.4).

RESULTS

The inclusion period started at July 15th, 2020 and ended with enrolment of the last patient on November 24th, 2020.

Among sixty-six patients contacted for a telephone screening, 34 patients (51.5%) were enrolled after informed consent was obtained as illustrated in **Figure 1**. Main reasons for non-enrolment included: did not own a smartphone or tablet (10.6%), unable to visit the outpatient clinic in the study period (9.1%) and interest in participating but did not send the signed informed consent form back to the investigator (9.1%). Enrolled patients were younger than excluded patients as illustrated in **Supplementary Table S1** but no

significant differences in gender, disease duration, SLAQ global health or SLEDAI were observed.

Most baseline characteristics were similar between the two intervention groups as presented in **Table 1**. However, a significant age difference was present as group WA → TS was slightly younger than group TS → WA i.e. mean age difference was -9.8 years, (95%CI: -19.3 to -0.2) and a p-value of 0.046 analysed with a two-sample t-test. As expected, most patients were women (79.4%), ANA positive (97.1%) and fulfilled the 2019 EULAR/ACR SLE Classification Criteria (1) (97.1%). One patient was ANA negative; thus, did not fulfil the 2019 classification criteria. However, the patient was diagnosed with renal biopsy lupus nephritis together with joint involvement, malar rash and hypocomplementemia; thus, the SLE diagnosis was not questioned.

A Bland-Altman plot showed excellent reliability and good agreement between the two device types for SLAQ Global Health **(Figure 2)**.

As presented in **Table 2**, equivalence was demonstrated for SLAQ Global Health between the two device types with a mean difference of -0.21, (95%CI: -0.65 to 0.23) as the 95%CI was well within the prespecified equivalence margin of ±0.75. Furthermore, equivalence was also shown for all other PROMs with prespecified equivalence margins (i.e. HAQ-DI, Pain VAS, and Fatigue VAS) except Patient Global Health VAS as the 95%CI of -1.18 to 6.53 exceeded the prespecified equivalence margin of ±5.0. However, as the difference in the Patient Global Health VAS score between the two device types was within the MCID of ±10.0, comparability was proven and the observed difference was not considered clinically relevant. Comparability with no statistically significant difference between the two device types was also demonstrated for SLAQ Total, SLAQ Worsening, PASS and Anchoring Question as presented in Table 2. However, a statistically significant difference between device types was observed for SLAQ Symptom of -0.56, (95%CI: -1.10 to 0.01), p-value 0.045. The observed difference was,

however, very small when considering the scale range of 0-24; thus, not judged to be of clinical relevance.

As presented in **Table 3**, no significant differences in gender or age groups was found when exploring subgroup analyses by SLAQ Global Health.

Patient preference for the DANBIO web app was very high 91.2% (31 patients), only 1 patient preferred the outpatient touchscreen (2.9%) and 2 patients had no device preference (5.9%).

DISCUSSION

To our knowledge, agreement between two electronic device types has not previously been demonstrated for reporting of PROMs by patients with SLE. Equivalence was shown for all PROMs with prespecified equivalence margins (i.e. HAQ-DI, Pain VAS, and Fatigue VAS) except Patient Global Health VAS where only comparability was proven. However, the observed difference in Patient Global Health VAS was within the limits of the MCID and not judged to have any clinical relevance. Comparability with no statistically significant difference between device types was also demonstrated for SLAQ Total, SLAQ Worsening, PASS and Anchoring Question; however, a statistically significant difference between device types was observed for SLAQ Symptom of -0.56, (95%CI: -1.10 to 0.01). The observed difference was, however, very small when considering the scale range of 0-24; thus, not judged to be of clinical relevance.

A recent systematic literature review (SLR) on mobile health apps for patients with SLE found a major lack of high-quality studies evaluating app efficacy (25). No apps used validated PROMs to evaluate symptoms and the educational content was labelled as low. The SLR only identified two RCTs; the first explored cellular text message reminders with educational content to increase adherence to outpatient visits among young adults with SLE and demonstrated improved adherence to clinic visits but not hydroxychloroquine treatment (26). The second study was a telephone-based weight

management program for people with physical disabilities and included only one patient with SLE (1.1%) (27). Thus, the SLR concluded that use of mobile health apps for patients with SLE is a relatively new and unexplored topic (25).

The findings in this trial are in line with previous studies in inflammatory arthritis that demonstrated agreement within the limits of defined MCIDs for various PROMs between two electronic device types (14,15). *Secher et al.* showed agreement in HAQ, Pain VAS, Fatigue VAS, Patient Global Health VAS, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) between a web-based solution using participants' own computer/tablet and an outpatient touchscreen by patients with rheumatoid arthritis (RA) or axial spondyloarthritis (axSpA) (14). Recently, agreement was demonstrated for HAQ-DI, Pain VAS, Fatigue VAS, Patient Global Health VAS, BASDAI, BASFI, PASS and anchoring question score between an app on the participants own device and an outpatient touchscreen by patients with RA, axSpA and psoriatic arthritis (PsA) (15).

Significant strengths to this study are the rate of responses by patients to all PROMs on the two device types, resulting in no missing data in both intervention groups; the study design i.e. randomised, crossover trial for which the internal validity is considered very high and the study population consisted mostly of females, judged to be representative for an outpatient SLE cohort.

In this trial, patients highly preferred the DANBIO web app over the outpatient touchscreen (91.2%). The preference was higher than previously reported: 78.3% of patients with RA, axSpA or PsA preferred the DANBIO app over the outpatient touchscreen (15) and 50% of patients with RA or axSpA preferred a from-home web-based solution on a computer/tablet over the outpatient touchscreen (14). A possible explanation for the high web app preference could be sampling bias as a significant difference in age was observed between excluded patients (i.e. patients who were not enrolled) and included patients. Another possible explanation for the high web app

preference could be easier access as the web app does not require being downloaded on participants' own devices in contrast to the previous DANBIO app. Moreover, in the study by *Secher et al.* participants were to answer PROMs on the web-based solution from home and not when and where it suited them as in this study.

Limitations to consider in this trial include the significant difference in age between excluded and included patients, as well as between intervention groups. This could be a result of sampling bias i.e. that older patients with less app experience/knowledge did not wish to participate in the trial. However, only 31.3% of excluded patients did not have access to or lacked smartphone/tablet technical skills. Age differences between the intervention groups were not considered to have influenced the trial results as each participant was his/her own control. Another possible limitation is that most participants had low disease activity (i.e. low SLEDAI, ds-DNA and CRP); thus, the PROM variance for the trial population would be less than in a population with high disease activity. However, 21.9% of the participants (7/32) had a SLEDAI > 6 corresponding to high disease activity (28) and 37.5% (12/32) were not in SLEDAI low disease activity (i.e. SLEDAI > 4 (29)). Moreover, it is unlikely that any variance in PROMs due to disease activity would affect the trial results in a significant way as the 95%CI for the PROM differences are well within the limits of the prespecified MCID. Another limitation could be insufficient power for the subgroup analyses on SLAQ Global Health; to minimise risk of reaching a false conclusion, it was decided that only a p-value of < 0.10 would be considered potentially important. No significant differences in subgroup analyses were demonstrated using this significant level. Finally, a limitation to consider is that three patients in the WA → TS group answered PROMs on the two device types without a washout period of one to two days i.e. the assessments were performed on two consecutive days resulting in a “washout period” under 24 hours. The reason for the deviation was simply that the patients forgot the scheduled PROM registration from home despite a text message reminder. However, as the PROM registrations was done on two

consecutive dates, the wash-out period was still longer than reported in similar studies (12–14,30–32).

Overall, the results of this trial i.e. agreement between two electronic device types for various PROMs by SLE patients are considered reliable; thus, the web app is an acceptable alternative for reporting PROMs in clinical practice. Moreover, a recent SLR by *Byrom et al*. found equivalence in PROM reporting when migrating from paper to electronic format and between different electronic device types (33). Thus, the results of this study can be generalised when implementing apps for PROM reporting in SLE management around the world and possibly also in diseases with similar symptom patterns e.g. vasculitis or mixed connective tissue disease. However, not all health care systems worldwide have access to the required technology to implement a web app; therefore, paper-based forms are still relevant.

Previous research has shown, that patients with SLE do not feel understood by their health care providers and have unvoiced concerns that are not met (34). PROMs can be a valuable tool to provide the physician with a better understanding of the patient's perception of disease state, and a web app allows patients to easily and conveniently report changes in disease activity as a flare occurs. Thereby, minimising the time delay from disease worsening to consultation with the treating physician. Implementation of this web app in clinical practice is expected to improve health care in SLE patients.

CONCLUSION

For the first time, equivalence and comparability using two electronic device types was demonstrated in various PROMs reported by patients with SLE. Moreover, patients strongly preferred use of the web app over the outpatient touchscreen. Implementation of this web app in clinical practice is expected to optimise the management of SLE patients.

ETHICS AND CONSENT

The local Ethics Committee and the Danish Data Protection Agency declared that approval was not required. However, the study was approved as a quality control trial by the Head of Hospital Management, Aalborg University Hospital. The trial was registered at Clinicaltrials.gov (NCT04411407) prior to participant inclusion (May 28th, 2020). Written informed consent was obtained from all participants before inclusion. The trial was carried out in accordance with the Helsinki Declaration, Good Clinical Practice (GCP) and the study protocol.

ACKNOWLEDGEMENTS

The authors thank patient research partner TAI for refining and approving the participant information material and approving the trial protocol. Furthermore, the authors thank data manager JHW for uploading the concealed allocation sequence in REDCap and MSc Christian Cato Holm for data management. PCT thanks the National Institute of Health Research for financial support to The NIHR Biomedical Research Centre in Musculoskeletal Disease, Oxford University Hospitals NHS Trust and University of Oxford.

FUNDING

The trial received financial support from the Danish Rheumatism Association (R192-A6737) and the Health Innovation Fond of North Denmark Region (2020-035538). The DANBIO web app is developed and owned by Zitelab ApS. The Oak Foundation supports the Parker Institute with a core grant (OCAY-18-774-OFIL). However, no funding parties nor Zitelab ApS were involved in the trial design or conduct, nor analyses or writing and submitting this article.

CONFLICT OF INTEREST

LD: Grants (BMS), Speakers bureau (Galderma, Eli Lilly, Janssen), ***PCT:*** Grants (Celgene, Eli Lilly, Galapagos, Gilead), Consultant (AbbVie, Biogen, Eli Lilly, Fresenius, Galapagos, Gilead, GlaxoSmithKline, Janssen, Nordic Pharma, Bristol-Myers Squibb, Pfizer, Roche, Sanofi), Speakers bureau (Biogen). ***VS***: Consultant (Abbvie, Amgen, AstraZeneca, BMS, EMD Serono, Equilium, Genentech/Roche, GSK, Horizon, Janssen, Lilly, Novartis, Pfizer, Rheos, Sanofi, Sun Pharma, UCB). **LU, *SH, JFP, RC, HBL, SJ, AV, JWG and SK:*** Declares no conflict of interest.

AUTHORS' CONTRIBUTION

LU, SK, LD and RC conceived the trial hypothesis and designed the trial. LU is the sponsor-investigator. LU, SH and JFP enrolled patients and via REDCap assigned participants to intervention groups. LU, SK, SH, JFP, LD and RC were responsible for the conduct of the trial, analyses and publication of trial data. LU wrote this article and all co-authors contributed with editing and approved the final draft.

DATA AVAILABILITY STATEMENT

This article and the supplementary information files include all analysed data from this study.

FIGURE LEGENDS

- **Figure 1:** Flow diagram of patient recruitment.
- **Figure 2A+2B:** Bland-Altman plot for SLAQ Global Health assessed on the two device types. ***Figure 2A:*** SLAQ Global Health web app scores against touchscreen scores i.e. x against y plot. Solid line: line of equality. ***Figure 2B:*** SLAQ Global Health difference (i.e. web app minus touchscreen) against mean SLAQ Global Health score. Solid horizontal line: mean difference, dashed horizontal lines: 95% limits of agreement.

REFERENCES

1. Aringer M, Costenbader K, Daikh D et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheumatol 2019; 71: 1400–12.
2. Leffers HCB, Troldborg A, Voss A et al. Smoking associates with distinct clinical phenotypes in patients with systemic lupus erythematosus: A nationwide Danish cross-sectional study. Lupus Sci Med 2021;8:e000474.
3. Annapureddy N, Devilliers H, Jolly M. Patient-reported outcomes in lupus clinical trials with biologics. Lupus 2016; 25: 1111–21.
4. Mahieu M, Yount S, Ramsey-Goldman R. Patient-Reported Outcomes in Systemic Lupus Erythematosus. Rheum Dis Clin North Am 2016; 42: 253–63.
5. Romero-Diaz J, Isenberg D, Ramsey-Goldman R. Measures of adult systemic lupus erythematosus: Updated Version of British Isles Lupus Assessment Group (BILAG 2004), European Consensus Lupus Activity Measurements (ECLAM), Systemic Lupus Activity Measure, Revised (SLAM-R), Systemic Lupus Activity Questionnaire for Population Studies (SLAQ), Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), and Systemic Lupus International Collaboration Clinics/American College of Rheumatology Damage Index (SDI). Arthritis Care Res 2011; 63: S37–46.
6. Katz P, Pedro S, Alemao E et al. Estimates of Responsiveness, Minimally Important Differences, and Patient Acceptable Symptom State in Five Patient-Reported Outcomes Measurement Information System Short Forms in Systemic Lupus Erythematosus. ACR Open Rheumatol 2020; 2: 53–60
7. Izadi Z, Gandrup J, Katz PP, Yazdany J. Patient-reported outcome measures for use in clinical trials of SLE: A review. Lupus Sci Med 2018; 5: e000279.
8. Karlson EW, Daltroy LH, Rivest C et al. Validation of a systemic lupus activity

questionnaire (SLAQ) for population studies. Lupus 2003; 12: 280–6.

9. Strand V, Gladman D, Isenberg D, Petri M, Smolen J, Tugwell P. Endpoints: Consensus recommendations from OMERACT IV. Lupus 2000; 9: 322–7.
10. Yazdany J, Yelin EH, Panopalis P, Trupin L, Julian L, Katz PP. Validation of the Systemic Lupus Erythematosus Activity Questionnaire in a Large Observational Cohort. Arthritis Rheum 2008; 59: 136–43.
11. Coons SJ, Eremenco S, Lundy JJ, O'Donohoe P, O'Gorman H, Malizia W. Capturing Patient-Reported Outcome (PRO) Data Electronically: The Past, Present, and Promise of ePRO Measurement in Clinical Trials. Patient 2015; 8: 301–9
12. Schefte DB, Hetland ML. An open-source, self-explanatory touch screen in routine care. Validity of filling in the Bath measures on Ankylosing Spondylitis Disease Activity Index, Function Index, the Health Assessment Questionnaire and Visual Analogue Scales in comparison with pap. Rheumatology. 2010;49:99–104.
13. Wæhrens EE, Amris K, Bartels EM et al. Agreement between touch-screen and paper-based patient-reported outcomes for patients with fibromyalgia: a randomized cross-over reproducibility study. Scand J Rheumatol 2015; 44: 503–10.
14. Secher AE, Glintborg B, Gudbergsen H et al. Comparing patient-reported outcomes entered at home versus at hospital, and testing touch screens for initial recruitment to scientific trials in arthritis patients. Scand J Rheumatol. 2019;48:178–84.
15. Uhrenholt L, Christensen R, Dreyer L, Schlemmer L, Hauge E-M, Krogh N, et al. Using a novel smartphone application for capturing of patient-reported outcome measures among patients with inflammatory arthritis: A randomized, crossover, agreement study. Scand J Rheumatol. 2021;1-9. Doi:

10.1080/03009742.2021.1907925.

16. Strand V, Boers M, Idzerda L et al. It's good to feel better but it's better to feel good and even better to feel good as soon as possible for as long as possible. Response criteria and the importance of change at OMERACT 10. J Rheumatol 2011;38:1720–7.
17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42: 377–81.
18. Harris PA, Taylor R, Minor BL et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019; 95: 103208.
19. Cook JA, Julious SA, Sones W et al. DELTA2 guidance on choosing the target difference and undertaking and reporting the sample size calculation for a randomised controlled trial. BMJ 2018; 363: k3750.
20. Moher D, Hopewell S, Schulz KF et al. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. BMJ 2010; 340: c869.
21. Dwan K, Li T, Altman DG, Elbourne D. CONSORT 2010 statement: Extension to randomised crossover trials. BMJ 2019; 366: l4378.
22. Christensen R, Bliddal H, Henriksen M. Enhancing the reporting and transparency of rheumatology research: a guide to reporting guidelines. Arthritis Res Ther 2013; 15: 109.
23. Piaggio G, Elbourne DR, Pocock SJ, Evans SJW, Altman DG, CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. JAMA 2012; 308: 2594–604.
24. Bland J, Altman D. Statistical methods for assessing agreement between two

methods of clinical measurement. Lancet 1986; 1: 307–10.

25. Dantas LO, Weber S, Osani MC, Bannuru RR, McAlindon TE, Kasturi S. Mobile health technologies for the management of systemic lupus erythematosus: a systematic review. Lupus 2020; 29: 144–56.
26. Ting TV, Kudalkar D, Nelson S et al. Usefulness of cellular text messaging for improving adherence among adolescents and young adults with systemic lupus erythematosus. J Rheumatol 2012; 39: 174–9.
27. Rimmer JH, Wang E, Pellegrini CA, Lullo C, Gerber BS. Telehealth weight management intervention for adults with physical disabilities: a randomized controlled trial. Am J Phys Med Rehabil 2013; 92: 1084–94.
28. Polachek A, Gladman DD, Su J, Urowitz MB. Defining Low Disease Activity in Systemic Lupus Erythematosus. Arthritis Care Res 2017;69:997–1003.
29. Gladman DD, Ibanez D, Urowitz MB. Systemic Lupus Erythematosus Disease Activity Index 2000. J Rheumatol 2002;29:288–91.
30. Epis OM, Casu C, Belloli L et al. Pixel or Paper? Validation of a Mobile Technology for Collecting Patient-Reported Outcomes in Rheumatoid Arthritis. JMIR Res Protoc 2016; 5: e219.
31. Richter JG, Becker A, Koch T et al. Self-assessments of patients via Tablet PC in routine patient care: Comparison with standardised paper questionnaires. Ann Rheum Dis 2008; 67: 1739–41.
32. Pincus T, Castrejon I, Riad M Obreja E, Lewis C, Krogh NS. Reliability, Feasibility, and Patient Acceptance of an Electronic Version of a Multidimensional Health Assessment Questionnaire for Routine Rheumatology Care: Validation and Patient Preference Study. JMIR Form Res 2020; 4: e15815.
33. Byrom B, Gwaltney C, Slagle A, Gnanasakthy A, Muehlhausen W. Measurement Equivalence of Patient-Reported Outcome Measures Migrated to Electronic Formats: A Review of Evidence and Recommendations for Clinical Trials and

Bring Your Own Device. Ther Innov Regul Sci 2019; 53: 426–30.

34. Hale ED, Treharne GJ, Lyons AC et al. “Joining the dots” for patients with systemic lupus erythematosus: Personal perspectives of health care from a qualitative study. Ann Rheum Dis 2006; 65: 585–9.