AALBORG UNIVERSITY

STUDENT REPORT

School of Medicine and Health

Patient-reported outcome measures collected via a web application versus a touchscreen in patients with Systemic Lupus Erythematosus

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Abstract

Introduction: In Denmark, patients with rheumatologic diseases have assessed patient-reported outcome measures (PROMs) via a touchscreen prior to each consultation in the outpatient clinic since 2006; however, as technology develops, interest in new ways of collecting PROMs is emerging. Bring your own device (BYOD) is a relatively new way of collecting PROMs through a personal electronic device. This study is evaluating the comparability between the national Danish Rheumatology Database (DANBIO) web app through a smartphone or a tablet and the traditional outpatient touchscreen regarding patients with Systemic Lupus Erythematosus (SLE).

Objectives: the aim of the study is to compare the outpatient touchscreen to a from home web app with Systemic Lupus Activity Questionnaire (SLAQ) global health as primary outcome.

Methods: This is a randomized, within-participants crossover, agreement study with enrolment of patients with SLE. Participants were randomized into two groups assessing PROMs through the two devices in a randomized order with a predefined wash out period. Differences in PROM scores with 95% confidence intervals (CI) were evaluated for similarity according to prespecified equivalence margins and a Bland-Altman plot was used to assess limits of agreement.

Results: Equivalence was found for SLAQ global health with a difference between the two electronic devices of -0.21, 95% CI (-0.64 to 0.23); Furthermore, all other PROMs were equivalent except for Visual Analogue Scale (VAS) global as the 95% CI of -1.45 to 6.80 exceeded the equivalence margin of ± 5. However, the difference was well within the minimal clinically important difference (MCID) of ± 10. Thirty-one (91.2%) of the total 34 participants preferred the DANBIO web app.

Conclusion: For the first time in patients with SLE, comparability between PROMs collected on a web app and an outpatient touchscreen was verified. Participants highly preferred the DANBIO web-app. Thus, the future implementation of the DANBIO web-app is expected to be a helpful and valuable tool for both patients and health care in order to monitor patients on a more individualized level.

Resume

Introduktion: Siden 2006 har det i Danmark været muligt for patienter med reumatologiske sygdomme at besvare spørgeskema, såkaldte patient-reported outcome measures (PROMs), omhandlende helbredsrelateret livskvalitet og funktionsevne. Aktuelt foregår indsamlingen af PROMs via en touchskærm i ambulatoriet. I takt med at teknologien har udviklet sig, er der opstået interesse for nye måder at indsamle PROMs på. En relativ ny måde at indrapportere på er via egen elektronisk enhed. Dette studie undersøger sammenligneligheden mellem indrapportering af PROMs hjemmefra via webappen fra den nationale Danske Reumatologiske Database (DANBIO) på tablet eller smartphone og indrapportering via den traditionelle ambulante touchskærm hos patienter med Systemisk Lupus Erythematosus (SLE).

Formål: Formålet med studiet er at sammenligne touchskærmen i ambulatoriet med DANBIO webappen besvaret hjemmefra med Systemic Lupus Activity Questionnaire (SLAQ) global health som det primære resultat.

Metode: Studiet er et randomiseret, overkrydsnings-, sammenlignelighedsstudie hos patienter med SLE. Deltagerne blev randomiseret i to grupper, der besvarede PROMs via webapp eller touchskærm i en randomiseret rækkefølge med en forudbestemt udvaskningsperiode. Forskelle i PROM-score med 95% konfidensintervaller (CI) blev evalueret for lighed i henhold til forudbestemte ækvivalensmargener, og et Bland-Altman-plot blev benyttet til at vurdere grænserne for sammenlignelighed.

Resultater: Mellem touchskærmen og webappen var der for SLAQ global health en forskel på -0,21, 95% CI (-0,64 til 0,23); således er disse ækvivalente. Desuden var alle andre PROMs ækvivalente med undtagelse af Visual Analogue Scale (VAS) global, hvor 95% CI på -1,45 til 6,80 overskred ækvivalensmargenen på ± 5. Forskellen var dog indenfor minimal clinically important difference (MCID) på ± 10. Af de i alt 34 deltagere foretrak 31 (91,2%) DANBIO webappen.

Konklusion: For første gang er sammenlignelighed af DANBIO webappen og den traditionelle touchskærm bekræftet hos patienter med SLE. Ækvivalens blev fundet for alle PROMs med undtagelse af VAS global, der dog var indenfor MCID. Deltagerne foretrak i høj grad DANBIO webappen, hvorfor den fremtidige implementering af DANBIO webappen forventes at være et nyttigt og værdifuldt værktøj for både patienter og sundhedssystemet til at monitorere patienter på et mere individualiseret niveau.

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease affecting multiple organs and causing a wide range of specific organ symptoms and non-specific symptoms that varies among patients and with disease activity [1]. These symptoms often have a significant impact on health-related quality of life (HRQoL). Thus, HRQoL is one of the important domains when monitoring patients with SLE. Therefore, evaluation of HRQoL as well as the following 3 important domains is recommended by Outcome Measures in Rheumatology (OMERACT) [2]: disease activity, organ damage and adverse events.

In Denmark, patients with SLE can report patient-reported outcome measures (PROMs) in the national Danish Rheumatology Database (DANBIO) at each consultation. PROMs are crucial for gaining an improved understanding of patients' interpretation of disease activity; however, PROMs are not a standard tool when assessing patients with SLE in clinical practice. Nevertheless, PROMs have been used in randomized controlled trials to evaluate patients with SLE [3], [4].

Some PROM questionnaires are specific for SLE and others are generic [4], [5]. At the moment, there are not international consensus about which PROM questionnaires are most preferable or essential concerning clinical management of patients with SLE. One of the increasingly used PROMs are Systemic Lupus Erythematosus Activity Questionnaire (SLAQ), which is a self-administered tool that evaluates the patient's own perception of lupus disease activity. It is previously shown, that SLAQ detects clinically significant disease activity and demonstrates good reliability and validity [5]–[7].

Over the years, different ways of collecting PROM data have been utilized; as technology has developed, so has assessment of PROMs from collecting data in paper form to digital solutions such as touchscreens and applications (apps) [8]. Previously, a touchscreen solution in the outpatient clinic was validated and implemented for patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) [9]. Moreover, a recent study from 2019 concerning patients with RA or axial spondyloarthritis (axSpA) concludes that answering PROMs via an outpatient touchscreen is comparable to answering PROMs via an electronic device from home [10]. However, interest in new digital solutions to collect PROM data through apps is emerging in healthcare. Bring your own device (BYOD) is a relatively new contribution of ways to collect digital PROMs. BYOD is built upon the idea of participants utilizing their own device to answer PROM questionnaires; thus, offering the patients a great freedom of choice to access and respond to PROMs on a website or via an app wherever and whenever it is suitable for the patient, which could lead to minimization of recall bias [8]. Furthermore, BYOD solution do not have the same disadvantages as the outpatient touchscreen such as queue, lack of discretion, hygienic problems, disturbances and unpleasant positions during data entering. Additionally, the patient will be able to report a disease flare immediately as it occurs. As a result, it is expected that PROMs via an app can be a screening tool to help clinicians triage and plan patient visits. This will limit unnecessary consultations in the outpatient clinic for patients in sustained remission and bring focus on the patients with threatening flares; thereby, improving health care.

The primary aim of this trial is to examine whether electronic assessment of SLAQ global health through the DANBIO web app is comparable to the outpatient touchscreen regarding patients with SLE.

Methods

Literature review

In the existing literature concerning rheumatology, two studies from Denmark elucidate ways of assessing PROMs; “Hetland et al.” compares the outpatient touchscreen to traditional paper form in patients with RA or AS [9] and “Secher et al.” compares the outpatient touchscreen to a web based solution on the participants own computer or tablet in patients with RA or axSpA [10]. However, to our knowledge there are no former studies regarding SLE and assessment of PROMs on different devices.

To investigate PROM assessments on different devices among patients with SLE a systematic search was performed in PubMed to evaluate the research area i.e. SLE and PROMs. ***Figure 1*** is a flowchart illustrating the search. Following search terms were used: “Systemic lupus erythematosus”, ”SLE”, ”Lupus”, ”PROM”, ”PROMS”, ”SLAQ”, ”Systemic lupus activity questionnaire”, “Patient reported outcome measure” and ”Patient reported outcome measures”. Limitations were set to English or Danish language and the search resulted in 218 articles. To find the final relevant articles, titles and abstracts were screened and if the articles were considered eligible, full texts were reviewed prior to full inclusion. Articles were considered eligible if they assessed PROM registration in patients with SLE. Thus, articles that did not evaluate these topics were excluded. In total, 12 full text articles were screened, and 8 articles were found relevant to elucidate the field.

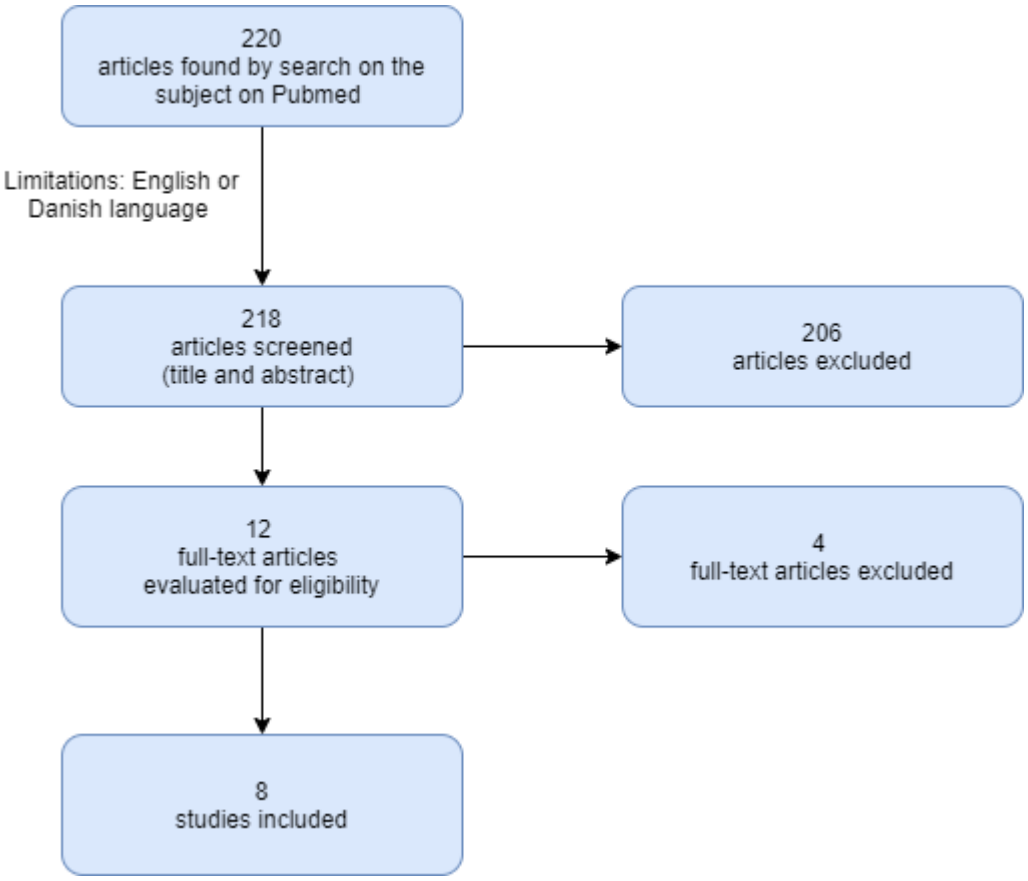

Figure 1: Flowchart of the literature search on Systemic Lupus Erythematosus and patient-reported outcome measures. Search was performed on the 28th of December 2020.

Patient research partner

Mutual understanding and shared knowledge can be achieved by collaboration between patients and health professionals during initiation and conduction of research trials [11].
After raising the research question, a patient research partner (PRP) was a part of the initial development of the study design and the written participant trial information.
The PRP was not involved in recruitment of patients nor conduction of the trial.

Study design and participants

The study is a randomized, within-participants crossover, agreement study. The participants were all aged ≥ 18 years and were enrolled at The Centre for SLE and Vasculitis at Aalborg University Hospital.
Inclusion criteria:

- Registered with the diagnosis SLE in DANBIO.
- Prior experience with PROM questionnaires in DANBIO (≥ 1 previous assessment).

Exclusion criteria:

- Inability to provide informed consent or to comply with the study protocol.
- Diagnosis of SLE of ≤ 12 months.
- No access to a device that can run the DANBIO web app.
- Not able to understand written Danish.

Procedures

The screening period lasted from the 15th of July 2020 to the 24th of November 2020. Patients with SLE at The Centre for SLE and Vasculitis at Aalborg University hospital who meet the eligibility criteria were contacted by phone and recruited for enrolment if they were interested in participating. After giving written informed consent, participants were randomized in ratio 1:1 into following two groups:

- ***Web app → Touchscreen (WA → TS):*** i.e. PROM data was reported through the DANBIO web app first and after a washout period secondly through the touchscreen in the outpatient clinic.
- ***Touchscreen → Web app (TS → WA):*** i.e. PROM data was reported through the touchscreen in the outpatient clinic first and after a washout period secondly through the DANBIO web app.

Due to minimization of recall bias, the washout period was set to one to two days between the two assessments. A text message reminder was sent if the participant did not answer the PROM assessment at the scheduled timepoint.
Participants were identified with civil registration number (CPR number) when reporting via touchscreen and with NemID when reporting via DANBIO web app through smartphone or tablet.

Objectives and outcomes

The aim of this trial was to examine whether electronic assessment through the DANBIO web app is comparable to the outpatient touchscreen in patients with SLE.
The primary outcome was SLAQ global health, which evaluates global assessment of lupus activity using a numerical rating scale score from 0-10.

Secondary outcomes were:

- *SLAQ worsening* evaluates presence or severity of lupus flare on a transitional scale e.g., 0 (no worsening), 1 (mild worsening), 2 (moderate worsening) or 3 (severe worsening). Minimal important clinically difference (MCID) is not defined.
- *SLAQ symptom score* evaluates the number of lupus specific symptoms present from 0-24. MCID is not defined.
- *SLAQ total score* evaluates severity of lupus disease activity by a weighted score of the 24 lupus specific symptoms, range 0-44. MCID is not defined.
- *(VAS) pain, VAS fatigue, and VAS global health* are measured on a horizontal VAS scale ranging from 0 mm (absence of symptoms) to 100 mm (maximum activity of the assessed parameter). The patient's answer is based on symptoms during the last week. MCID is defined as ± 10 mm i.e., equivalence margin of ± 5 mm [12].
- *Patient Acceptable Symptom State (PASS)* consists of one question concerning symptom state during the last 48 hours and is answered with "yes" or "no".
- *Anchoring question* elucidates change in disease activity since the last visit at the outpatient clinic. One of the following options is chosen: much worse (-3), worse (-2), slightly worse (-1), unchanged (0), slightly better (1), better (2) or much better (3).
- *HAQ-DI* assesses the patient's physical function and is answered on a scale from zero (no disability) to three (completely disabled). MCID is defined as ± 0.22 points i.e., equivalence margin of ± 0.11 points [12].

Finally, participants were asked about device preference.

Demographic variables

In addition to the measures listed above, demographic data was collected from the patient's electronic medical record and/or the DANBIO database. Demographics included gender, age, disease duration, current treatment for SLE and latest values for the following: SLEDAI activity score, SLICC damage index, classification criteria registration, HAQ-DI, VAS pain, VAS fatigue, VAS global assessment, PASS, anchoring question, and SLAQ scores. In addition, ANA positivity, latest CRP, latest ds-DNA, latest C3 and C4 value were registered.

Subgroup analyses

Subgroup analyses for the primary outcome SLAQ global health were made in order to elucidate potential confounders when answering SLAQ global health. Analyses were performed in the following subgroups: "Female vs. Male", "The younger half vs. The older half" (respectively younger or older than the median age), "Age < 65 years vs. Age ≥ 65 years".

Ethics

This study was considered a quality control study. Therefore, approval was not required by the Ethics committee (case number: 73960) nor the Danish Data Protection Agency. Prior to inclusion, the study was registered at Clinicaltrials.gov (NCT04411407). Before enrolment, written informed consent were obtained from all participants and the trial was carried out in compliance with the protocol and Helsinki Declaration.

Power and sample size calculation

In the existing literature, there was not found any explicit MCID for SLAQ global health. Therefore, a biostatistician with no clinical involvement in the study, estimated a standard deviation (SD) from 1000 random bootstrap samples of SLAQ global health estimates from a sample of 44 patients with SLE from Aalborg University Hospital. The median SD was 2.99 (range: 2.25-3.62); thus, as the MCID is defined as half of the SD, the MCID = 0.5×2.99 = 1.495.

Equivalence between two interventions is defined as half of the MCID; therefore, as 1.495/2 = 0.75 the equivalence margin for SLAQ global health must be ±0.75. A more conservative estimate of the equivalence margins for SLAQ global health that allows minimal variance between two interventions can be calculated using the minimum value of the SD range of 2.25. Thus, the conservative/strict equivalence margins are: (0.5×2.25)/2 = ± 0.56.

In a two one-sided tests analysis for additive equivalence of paired means with bounds ±0.56 for the mean difference in SLAQ global health and a significance level of 0.05, assuming a mean difference of 0 SLAQ global health points, a common standard deviation of 3.0 and correlation 0.95 (between measures), a sample size of 33 patients is 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 group.

Allocation concealment and implementation

Prior to enrolment of participants, a computer-generated randomization sequence was created by a biostatistician using SAS PROC PLAN. Participants were distributed in permuted blocks of 2 to 4. The randomization was made with a 1:1 allocation ratio. Afterwards, a data manager, with no clinical involvement in the study, entered the randomization sequence into the e-CRF in the Research Electronic Data Capture Database (REDCap).

Statistical analysis

Normal distributed demographic variables were analyzed by calculating mean and standard deviation (SD), which is an expression of the variance in the data. Demographic variables that were not normal distributed were analyzed with median and interquartile range (IQR), which is a measure of statistical dispersion. Binary variables were listed as number and percentage.

A paired t-test was used to calculate the mean SLAQ global health score for the two devices and the difference in SLAQ global health score with a 95% confidence interval (CI). A Bland-Altman plot was used to assess limits of agreement (LoA). VAS pain, VAS fatigue, VAS global and HAQ-DI were also assessed using a paired t-test.

A Wilcoxon signed-rank test was used to test the hypothesis of no difference between the two devices for PASS and anchoring question.

Two sample t-test subgroup analyses were performed on SLAQ global health to find potentially difference in factors. Due to the relatively small sample size in the subgroups, the analyses are probably not adequately powered. Therefore, only a p-value <0.10 were held potentially important.

Results

Enrolled vs. not enrolled patients

As illustrated in ***figure 2,*** a total of 66 patients with SLE were contacted by phone and 34 patients were enrolled in the trial. An overview of patient recruitment and reasons for exclusion are illustrated. Furthermore, it is seen that all participants answered both web app and touchscreen.

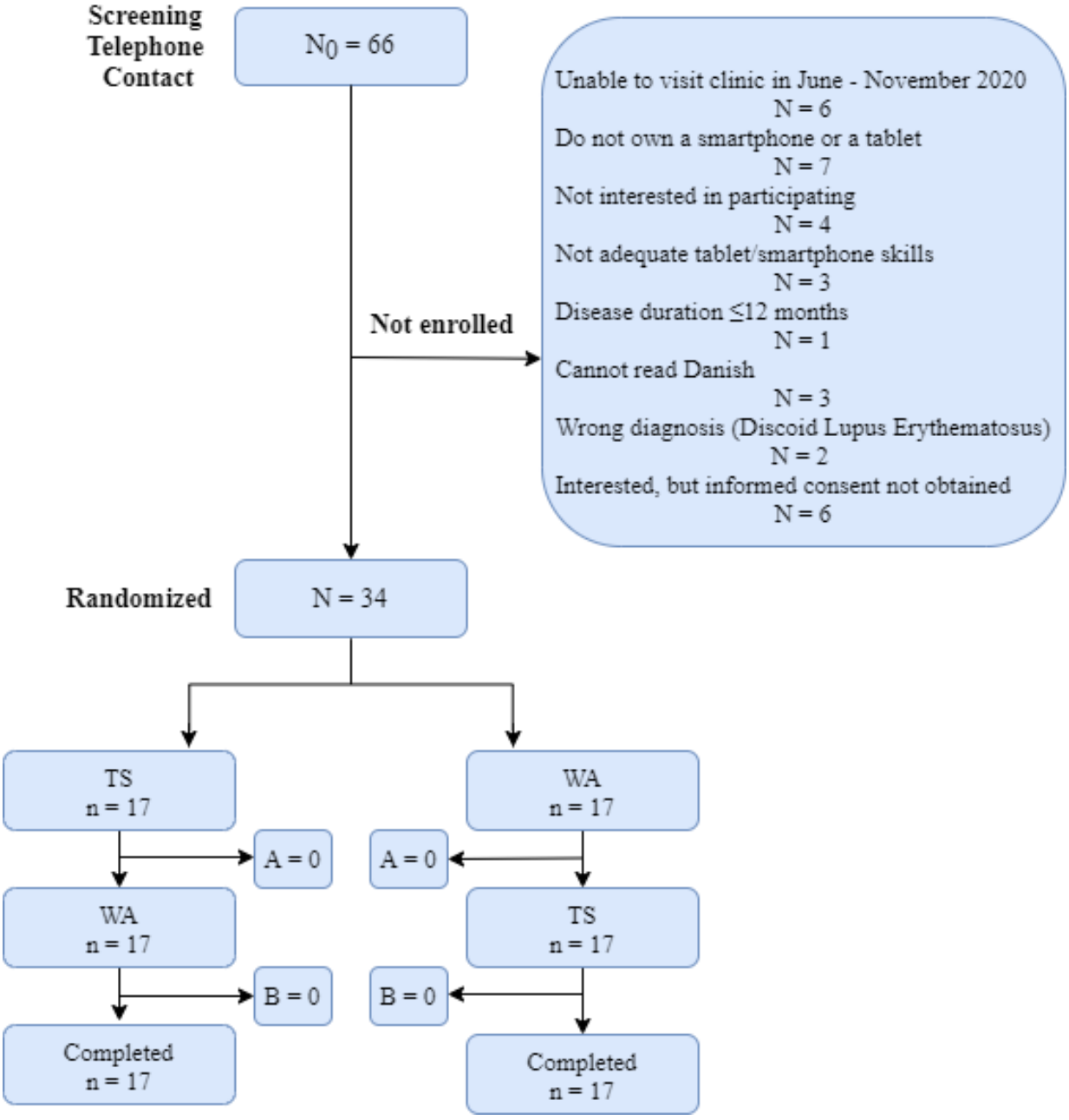

Figure 1: Enrolment and randomization process.
n is based on successful collection of SLAQ global health.
WA: Web app. TS: Touchscreen. A: First device registration not done, incomplete first data registration, withdrawal/lost to follow-up. B: Second device registration not done, incomplete second data registration, withdrawal/lost to follow-up.

As shown in ***table 1*** there were no significant differences in gender, disease duration, previous SLAQ global health and previous SLEDAI between enrolled patients and not enrolled patients. However, there was a significant difference in age (p-value of 0.02) between enrolled and not enrolled patients. The following baseline values were missing: SLAQ global health: enrolled (n = 2), not enrolled (n = 15) and SLEDAI: enrolled (n = 2), not enrolled (n = 14).

Table 1: Comparison between screened patients stratified by enrolment

	Enrolled n = 34 (51.5%)	**Not enrolled n = 32 (48,5%)**	**P-value**
Female[1], n (%)	27 (79.4)	24 (75.0)	0.67
Age in years, mean (SD)	46.5 (14.4)	55.4 (15.3)	0.02
Disease duration in years, median (IQR)	76.5 (24.5-155.5)	129.5 (56.5-236.0)	0.07
SLAQ global health, median (IQR)	3.0 (1.0-5.8)	5.0 (1.0-7.5)	0.28
SLEDAI, median (IQR)	2.0 (0.0-6.0)	2.5 (0.0-6.0)	0.86

N: number of patients. SD: Standard deviation. SLAQ: Systemic Lupus Activity Questionnaire. SLEDAI: Systemic Lupus Erythematosus Disease Activity Index. IQR: Interquartile range.

Demographics

Patient demographics are shown in ***table 2***. Generally, the baseline values in the two groups are similar with no major differences in gender, classification criteria, SLAQ, SLICC etc. However, some differences were found in age, disease duration, latest SLEDAI and latest ds-DNA. Only few baseline values were missing: One missing value for PASS in group WA → TS. Two missing values for SLEDAI in group WA → TS. Two missing values for SLAQ global health, SLAQ symptom score, SLAQ total score, SLAQ worsening in group WA → TS. One missing value for Anchoring question in group WA → TS.

Table 2: Patient demographics and clinical characteristics.			
Variable	**WA → TS n = 17**	**TS → WA n = 17**	**All n = 34**
General characteristics			
Women, n (%)	14 (82.4)	13 (76.5)	27 (79.4)
Age (years), mean (SD)	41.6 (13.4)	51.4 (13.9)	46.5 (14.4)
Fulfil 2019 EULAR/ACR SLE Classification Criteria, n (%)	16 (94.1)	17 (100)	33 (97.1)
Disease duration (month), median (IQR)	92 (20-158)	67 (26-193.5)	76.5 (24.5-155.5)
Latest SLEDAI, median (IQR)	6.0 (0.0-8.0)	1.0 (0.0-4.5)	2.0 (0.0-6.0)
Latest SLICC Damage Index, median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)
ANA positive, n (%)	16 (94.1)	17 (100)	33 (97.1)
Latest ds-DNA, median (IQR)	9.6 (3.4-41.0)	3.6 (0.9-14.5)	7.5 (1.0-15.8)
Latest c3, mean (SD)	1.0 (0.2)	1.0 (0.4)	1.0 (0.3)
Latest c4, mean (SD)	0.2 (0.1)	0.2 (0.1)	0.2 (0.1)
Latest CRP (mg/L), median (IQR)	3.4 (1.3-7.2)	1.6 (1.0-4.4)	2.4 (1.2-5.1)
Current medication for SLE			
None, n (%)	4 (23.5)	2 (11.8)	6 (17.7)
Hydroxychloroquine, n (%)	11 (64.7)	13 (76.5)	24 (70.6)
Azathioprine, n (%)	2 (11.8)	3 (17.7)	5 (14.7)
Prednisolone, n (%)	5 (29.4)	5 (29.4)	10 (29.4)
Methotrexate, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Mycophenolate mofetil, n (%)	2 (11.8)	1 (5.9)	3 (8.8)
Rituximab, n (%)	0 (0.0)	1 (5.9)	1 (2.9)
Cyclophosphamide, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Cyclosporine, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Tacrolimus, n (%)	0 (0.0)	2 (11.8)	2 (5.9)
Belimumab, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Other, n (%)	0 (0.0)	1 (5.9)	1 (2.9)
Current RAS blocker			
None, n (%)	11 (64.7)	11 (64.7)	22 (64.7)
ACE-inhibitor, n (%)	4 (23.5)	4 (23.5)	8 (23.5)
Angiotensin II receptor blockers, n (%)	2 (11.8)	2 (11.8)	4 (11.8)
PROMs			
SLAQ global health, median (IQR)	3.0 (1.0-6.0)	4.0 (1.0-5.5)	3.0 (1.0-5.8)
SLAQ symptom score, median (IQR)	10.0 (7.0-12.0)	11.0 (6.5-17.0)	10.5 (7.0-14.0)
SLAQ total score, median (IQR)	9.3 (5.8-15.3)	11.0 (5.6-16.4)	10.3 (5.8-16.2)
SLAQ worsening, median (IQR)	0.0 (-2.0-0.0)	0.0 (0.0-0.0)	0.0 (-1.0-0.0)
HAQ-DI, median (IQR)	0.1(0.0-0.7)	0.3 (0.1-1.1)	0.3 (0.0-0.8)
VAS pain (0-100 mm), median (IQR)	17.0 (5.5-53.0)	24.0 (6.0-53.5)	18.5 (5.8-53.3)
VAS fatigue (0-100 mm), median (IQR)	30.0 (15.5-71.0)	54.0 (32.0-75.5	48.0 (17.8-74.3)
VAS global (0-100 mm), median (IQR)	46.0 (8.5-60.0)	50.0 (11.0-67.0)	48.0 (8.8-65.0)
PASS “Yes”, n (%)	13 (81.3)	13 (76.5)	26 (78.8)
Anchoring question, median (IQR)	0.0 (-0.8-0.0)	0.0 (-0.5-0.0)	0.0 (-0.5-0.0)

WA: Web app, TS: Touchscreen. N: Number of patients. SD: Standard deviation. SLE: Systemic Lupus erythematosus. EULAR: European League Against Rheumatism. ACR: American College of Rheumatology. SLICC: Systemic Lupus International Collaborating Clinics. ANA: Antinuclear antibodies. Ds-DNA: Double stranded deoxyribonucleic acid. C3: Complement component 3. C4: Complement component 4. CRP: C-reactive Protein. RAS: Renin-angiotensin System. ACE: Angiotensin Converting Enzyme. SLAQ: Systemic Lupus Activity Questionnaire. HAQ-DI: Health Assessment Questionnaire Disability Index. VAS: Visual Analogue Scale. PASS: Patient Acceptable Symptom State. IQR: Interquartile range.

Primary and secondary outcomes

The analyses in ***Table 3*** shows that SLAQ global health scores between the two devices has a mean difference of -0.21, 95% CI of -0.64 to 0.23; thus, this is under the equivalence margin of ± 0.75 for SLAQ global health. Equivalence was also demonstrated for all other PROMs except for VAS global as the 95% CI of -1.45 to 6.80 exceeded the equivalence margin of ± 5. However, the difference between the two devices for VAS global lies well within the MCID of ± 10; therefore, the difference does not have any clinical relevance.

Twenty-five patients (73.5%) had a difference in PASS of 0; thus, had the same answer on both devices. Wilcoxon signed rank test showed a p-value of 0.74 i.e. no statistical difference between the two devices. Similarly, 26 patients (76.5%) answered the same on the anchoring question yielding a p-value of 0.16. Twenty-eight patients (82.4%) had no difference in SLAQ worsening with a p-value of 0.10, hence, no statistical significance.

Table 3: Comparison between devices for all PROM and clinical outcomes.

Outcome	**WA → TS**		**TS → WA**		**Difference**	
Primary outcome	***Mean***	***SD***	***Mean***	***SD***	***Mean difference***	***95% CI***
SLAQ global health	3.1	2.6	3.3	2.7	-0.21	-0.64 to 0.23
Secondary outcomes						
SLAQ symptom score	10.1	5.5	10.6	5.3	-0.56	-1.10 to -0.02
SLAQ total score	10.5	7.3	11.1	7.1	-0.61	-1.48 to 0.25
HAQ-DI, (0-3)	0.41	0.54	0.40	0.52	0.02	-0.01 to 0.05
VAS pain (0-100 mm)	24.9	26.5	22.9	22.5	2.0	-0.86 to 4.86
VAS fatigue (0-100 mm)	46.8	33.6	47.1	30.2	-0.3	-3.75 to 3.10
VAS global (0-100 mm)	31.0	27.1	28.3	26.7	2.7	-1.45 to 6.80

WA: Web app. TS: Touchscreen. SD: Standard deviation. CI: Confidence interval. SLAQ: Systemic Lupus Activity Questionnaire. HAQ-DI: Health Assessment Questionnaire Disability Index. VAS: Visual Analogue Scale.

Figure 3 demonstrates agreement between the two devices for the primary outcome SLAQ global health. One out of 34 patients is outside the level of agreement corresponding to 2.9%. Thus, as this is under 5%, agreement between the DANBIO web app and the touchscreen was demonstrated.

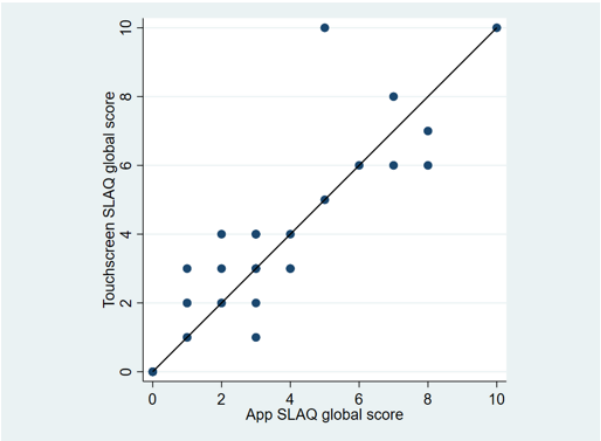

Figure 3A: Bland-Altman XY-plot illustrating SLAQ global health scores assessed with the two devices with a line of equality i.e. x = y.

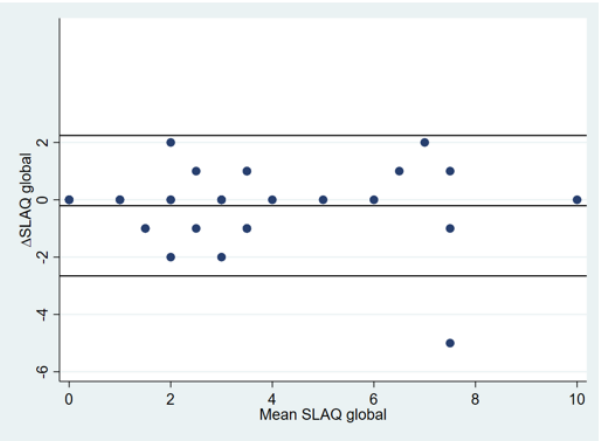

Figure 2B: Bland-Altman plot showing SLAQ global health difference against SLAQ global health mean with lines showing the mean difference and 95% limits of agreement. One outliner is seen corresponding to 2.9%.

When analysing device preference; 31 (91.2%) patients preferred the DANBIO web app, 2 (5.9%) patients had no device preference and 1 (2.9%) patient highly preferred the touchscreen.

Subgroup analyses

Subgroup analyses for the primary outcome SLAQ global health, presented in ***table 4***, shows no significant difference in gender or age for enrolled patients.

Outline Table 4: Results of stratified (subgroup) analyses for SLAQ global health (the primary outcome).

Subgroups	**Subgroup "Yes"**			**Subgroup "No"**			**Difference between subgroups**		
	n	***Mean***	***SD***	***n***	***Mean***	***SD***	***Mean***	***95% CI***	***p value***
Yes = Female sex No = male sex	27	-0.1	1.3	7	-0.6	1.0	0.5	-0.6 to 1.5	0.39
Yes = The younger half (< 47 years) No = The older half (≥ 47 years)	17	0.0	0.6	17	-0.4	1.7	0.4	-0.5 to 1.3	0.34
Yes = Age < 65 years No = Age ≥ 65 years	31	-0.1	1.3	3	-1.0	1.0	0.9	-0.7 to 2.4	0.26

SD: Standard deviation. CI: Confidence interval. n: Number of patients.

Discussion

This study found comparability between SLAQ global health in DANBIO web app and the outpatient touchscreen. To our knowledge, this study is the first to demonstrate that the two devices can be utilized interchangeably for assessing PROM's in patients with SLE.

The assessment of patients with SLE in clinical trials should involve patient-reported outcomes, including a global assessment and specific instruments that capture the impact of the disease on the patient quality of life. SLAQ has previously demonstrated good validity and reliability, and has been employed in four different languages (German, Italian, Japanese and English) [6], [7], [13], [14]. This study demonstrates a feasible tool that encourages PROMs to be captured in patients with SLE.

The findings of the study is in line with previous findings by Secher et al. whom found no clinically relevant differences in HAQ-DI, VAS pain, VAS fatigue, VAS global, between a web-based from home solution and the outpatient touchscreen among patients with RA or axSpA [10].

Furthermore, 31 (91.2%) of the total 34 enrolled patients preferred the web app. In contrast, Secher et al [10], who compared the out-patient touchscreen to tablet or computer from home, found that 50% of patients preferred reporting PROMs from home. Hence, our higher web app preference indicates that patients prefers answering from home via smartphone or tablet to a higher degree than answering from home via computer or tablet. A reason for this could be the easy assessment to a smartphone or tablet compared to a computer. Nevertheless, one must take into consideration that one of our patients (2.9%) preferred the touchscreen and two (5.9%) patients had no preference. Furthermore, ten of the not enrolled patients were excluded due to different reasons regarding responding via the web app such as lacking technical skills or not owning a suitable electronic device. This can probably be explained by the age difference between the enrolled and not enrolled patients (p-value 0.02). Thus, the touchscreen must remain an option for those patients who will most likely not utilize the web app.

Presumably, there are many reasons for the web app preference and an important advantage is better hygienic conditions regarding the web app leading to lower rates of transmission of infectious diseases. Other disadvantages regarding use of the touchscreen such as queue, lack of discretion, disturbance and unpleasant positions during data entering will be avoided when implementing the web app, which can be other explanations for the web app preference.

Furthermore, we had three patients who were not enrolled because they could not read Danish either due to dyslexia or due to different ethnic background. One can imagine that such patients will benefit from the web app, as there are several tools available for electronic devices that help with translation and recitation.

Despite a significant difference in disease duration, age, disease activity and ds-DNA between the two intervention groups the results show comparability in PROMs between the two devices. This indicates that the web app can be used safely regardless of age, disease duration and disease activity.

We had a response rate of 100 percent among the participants, hence no missing data on the PROM assessments. However, this study does have limitations to discuss; only 34 out of 66 screened patients were enrolled, which can lead to sampling bias; thereby, undermining the external validity of the trial. Nevertheless, there was no significant difference in gender, previous SLAQ global health and previous SLEDAI between enrolled patients and not enrolled patients, but there was a significant difference in age (p-value: 0.02). One should consider whether this difference would have an impact on the results, e.g. it is imaginable that younger patients are more likely to prefer the web app. Additionally, it could be interesting to investigate whether other factors such as socioeconomic status, educational level or disease severity would matter. However, a study from Puerto Rico finds that disease activity status do not have an impact on whether the patient's wishes to participate in scientific trials or not [15].

Furthermore, one of our secondary outcomes, VAS global, was not statistical equivalent as the 95% CI of -1.45 to 6.80 exceeded the equivalence margin of ±5. Nevertheless, VAS global lies within the boundaries for MCID **(**±10); which makes it assumable, that it has no clinical relevance.

The subgroup analyses show no statistically significant differences. However, a possible limitation regarding our subgroup analyses is that the subgroups may not be adequately powered; in consequence, a p-value of < 0.10 was considered potentially important and no important differences were observed in the subgroup analyses.

We had three patients whose wash-out periods were shorter than stated in the protocol which can lead to recall bias. However, none of the patients carried out their assessments on the same day and the wash-out period for the mentioned patients was still longer than the wash-out periods carried out in similar studies regarding PROM assessments in rheumatic patients, where the registered wash-out periods were decided to be between 5 minutes and 24 hours [9], [10], [16]–[19]. Overall, we believe that the findings of this study are fair to be considered reliable.

PROMs are essential in the management of multiple diseases including SLE as former research has identified a disconnect between physician and patient perception of the disease. [20]–[22]. Thus, PROMs are crucial for gaining improved understanding of the impact of the disease on the patients' quality of life and early assessment of disease activity. If the patients can report enhanced disease activity from the very beginning of a flare from home, the delay time from disease worsening to contact with a physician will decrease. High patient preference for the web app shows that there is a great interest and need for digital PROM assessment among patients with SLE.

Conclusion

This study demonstrates that the DANBIO web app is a valid tool for reporting PROMs in patients with SLE. For the first time, equivalence between a web app and an outpatient touchscreen was verified for SLAQ and several other PROMs for patients with SLE. Patient preference for the DANBIO web app was very convincing. Future implementation of the DANBIO web app is considered safe for patients with SLE, and the web app is expected to help physicians triage outpatient visits. Thus, implementation of the web app is considered a helpful tool for healthcare and the individual patient.

Rheumatology Key Messages

- The DANBIO web app is comparable to the outpatient touchscreen regarding patients with SLE.
- The DANBIO web app has several advantages compared to the outpatient touchscreen.
- This study is the first to evaluate PROM assessments regarding patients with SLE.

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