

### Telemedicine for Patients with Systemic Lupus Erythematosus in a Publicly Funded Hospital System: A Retrospective Study

Sebastian Bruera, Kristen Andrews Staggers, Maria Eugenia Suarez-Almazor, Sandeep Krishna Agarwal

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### Table of Contents

Original Manuscript	. 4
Supplementary Files	25

# Telemedicine for Patients with Systemic Lupus Erythematosus in a Publicly Funded Hospital System: A Retrospective Study

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#### Abstract

**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that requires frequent clinic and laboratory visits. However, patients with SLE, particularly those that are under-resourced, have unacceptably high rates of no-shows.

**Objective:** The objective of this study was to determine no-show rates associated with telemedicine visits during the COVID-19 pandemic in comparison to no show rates associated with contemporaneous and historic in-person.

**Methods:** We performed a retrospective cohort study in a publicly funded county hospital system in Houston, Texas. We identified a cohort of established SLE patients by International Classification of Diagnosis (ICD) codes that were independently confirmed as SLE by review of medical records. We identified patients who were seen from March to December in 2018, 2019, and 2020 (to reflect the height of the COVID-19 pandemic and account for seasonal changes in disease activity). Our primary outcome was percentage of no-shows for rheumatology clinic appointments. Our secondary outcome was laboratory utilization adherence, which was defined as lupus-specific blood and urine studies conducted within 30 days of the scheduled appointment. Covariates included age, gender, race, ethnicity, and SLE-related prescription drugs.

**Results:** We included 156 SLE patients in our analysis. Most were female (90.4%), Hispanic (49.3%) and had a median age of 43. In 2020, the no-show rate for telemedicine was 5.5% compared to a no-show rate of 16.2% for in-person visits (p=0.002). After multivariable adjustment for covariates, the odds of no-show was lower for telemedicine visits (OR 0.39, 95% CI 0.20-0.77). There were no differences in adherence to laboratory testing.

**Conclusions:** Telemedicine visits had decreased odds of no-shows without difference in laboratory testing adherence after adjustment for covariates. More research is needed to determine the clinical impact of telemedicine on patients with SLE. ?

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## **Original Manuscript**

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Running head: Telemedicine outcomes in Systemic Lupus Erythematosus

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#### Abstract

#### **Background**

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that requires frequent clinic and laboratory visits. However, patients with SLE, particularly those that are under-resourced, have unacceptably high rates of no-shows.

#### **Objectives**

The objective of this study was to determine no-show rates associated with telemedicine visits during the COVID-19 pandemic in comparison to no show rates associated with contemporaneous and historic in-person.

#### **Methods**

We performed a retrospective cohort study in a publicly funded county hospital system in Houston, Texas. We identified a cohort of established SLE patients by International Classification of Diagnosis (ICD) codes that were independently confirmed as SLE by review of medical records. We identified patients who were seen from March to December in 2018, 2019, and 2020 (to reflect the height of the COVID-19 pandemic and account for seasonal changes in disease activity). Our primary outcome was percentage of no-shows for rheumatology clinic appointments. Our secondary outcome was laboratory utilization adherence, which was defined as lupus-specific blood and urine studies conducted within 30 days of the scheduled appointment. Covariates included age, gender, race, ethnicity, and SLE-related prescription drugs.

#### Results

We included 156 SLE patients in our analysis. Most were female (90.4%), Hispanic (49.3%) and had a median age of 43. In 2020, the no-show rate for telemedicine was 5.5% compared to a no-show rate of 16.2% for in-person visits (p=0.002). After multivariable adjustment for covariates, the odds of no-show was lower for telemedicine visits (OR 0.39, 95% CI 0.20-0.77). There were no differences in adherence to laboratory testing.

#### **Conclusions**

Telemedicine visits had decreased odds of no-shows without difference in laboratory testing adherence after adjustment for covariates. More research is needed to determine the clinical impact of telemedicine on patients with SLE.

#### **Background**

The Coronavirus Disease 2019 (COVID-19) pandemic triggered a widespread and emergent use of telemedicine as an option for patients to avoid exposure to the SARS-CoV-2 virus.[1-2] The use of telemedicine has been especially important in patients with chronic diseases, such as systemic lupus erythematosus (SLE), who are at a high risk of severe COVID-19 and may benefit from less public exposure.[3-4] Missed appointments in general are associated with an increased risk of mortality and adverse outcomes.[5-7] Telemedicine the a potential benefit of improving no-shows by making clinic visits more accessible. This may be particularly important for patients in lower socioeconomic status (SES) who may have difficulties attending visits because of transportation, work, or financial factors. Yet, it has been suggested that telemedicine services are less likely to be used in lower socioeconomic status populations. [8-9]

Despite the potential advantages of telemedicine, especially for patients of low SES, there are still important concerns, which should be considered when telemedicine is implemented for patients with SLE. First, patients with SLE are usually followed every three to four months and require serial evaluations including blood pressure monitoring, physical examination and clinical laboratory tests – regardless of the presence or absence of symptoms or examination findings.[10]It is unclear how telemedicine may affect adherence to visits and adherence to laboratory testing since patients may be more likely to obtain blood work if they are already at the clinic site.

We performed a retrospective cohort study in patients with SLE managed in a county hospital system in Houston, TX. This population is highly diverse, with most patients being underinsured or uninsured and low SES. We hypothesized that SLE patients in this system will have lower no-show rates with telemedicine modalities, such as telephone and video visits, compared to in person visits. Furthermore, we explored patient characteristics (such as medications and age) and their association with visit types. We also examined the impact of telemedicine on patients' adherence to laboratory testing.

#### Methods

Design and patient population

We performed a retrospective analysis of patients with SLE seen in the Harris Health System (HHS). The HHS is a fully integrated healthcare system that provides care to residents of Harris County, Texas, which has an estimated population of 4.7 million.[11] The patient population at HHS includes 54% who are uninsured, 22% who have Medicaid, 12% who have Medicare, and 13% who have private insurance. Most uninsured patients qualify for HHS insurance ("the gold card") that provides partial or full reimbursement for care to patients with a household income that does not exceed 150% of the federal poverty level. Once a patient receives a gold card, the co-pay for any visits is dictated by income stratification and ranges.

#### Patient selection

We identified a cohort of established SLE patients using International Classification of Diagnosis (ICD) 10 diagnostic codes (M32.x, excluding M32.0). SLE patients were included if they were seen at the HHS rheumatology clinics by a rheumatologist at least once between March and September 2020 (at a time when telemedicine was implemented because of the pandemic). Data was initially collected through the information technology services provided by HHS. Patients were seen at a large HHS rheumatology teaching clinic staffed by seven rheumatologists. The diagnosis of SLE was independently confirmed by chart review by a rheumatologist (SB) if they met the American College of Rheumatology 2019 diagnostic criteria. Patients were offered telemedicine visits either by telephone encounters or by video with a secured third-party platform (Doximity). Between March 2020 – September 2020 the HHS rheumatology clinic offered both in-person visits along with telemedicine encounters. The decision to have a telemedicine versus in-person encounter was driven by patient preference.

As controls, we identified cohorts of SLE patients seen in the HHS rheumatology clinic from March to September of 2018 and 2019 (pre-pandemic). We limited the control cohort to SLE

patients seen from March to September to account for potential seasonal changes in practice patterns and disease activity, which have been previously described.[12] We also identified a subgroup for analysis of patients that were seen at least once in both 2019 and in 2020. This subgroup analysis of "no-shows" was performed to examine trends for the same patients who had attended at least one follow-up appointment each year.

#### **Outcomes**

Our primary outcome was the percentage of no-shows for rheumatology clinic follow-up appointments. No-shows were defined as visits for which patients did not show up, or that were canceled by the patient within the same day. Clinic visits rescheduled by patients prior to 24 hours before the clinic appointment were not considered as no-shows. Secondary outcomes included laboratory testing utilization including complete blood count (CBC), comprehensive metabolic panel (CMP), urinalysis, serum complement levels (C3 and C4), and serum titers of anti-double stranded DNA (anti-dsDNA) antibodies within 30 days before or after each completed clinic visit. It is the standard in the rheumatology clinics that all SLE patients obtain laboratory testing and have a clinic appointment *at least* every three months, regardless of disease activity.[10] All laboratory studies for patients seen at HHS clinics are done within the HHS at one of 17 clinics or two large hospitals. Laboratory tests can be ordered as a pre-clinic lab (performed within 14 days of a clinic appointment) or obtained the day of their clinic visit. For telemedicine encounters, blood work can be obtained pre-clinic or at patients' convenience for any day of their preference at the closest HHS clinical laboratory.

#### **Covariates**

Baseline demographics included age, gender, race, ethnicity, and utilization of SLE-related prescribed drugs at the initial visit in the period of interest. We included baseline demographics as a covariate due to multiple studies showing differences in digital literacy amongst patients of different ages, race, and ethnicity.[13] The insurance coverage for each specific visit appointment was not

available, as insurance status can change over time, however, as previously mentioned, over 85% patients that are seen in our clinics are uninsured or publicly insured.

We also included whether patients were prescribed SLE-specific drugs (hydroxychloroquine, mycophenolate, azathioprine, methotrexate, rituximab, belimumab, tacrolimus, prednisone, and cyclophosphamide) in 2018, 2019, or 2020. Our data includes medications prescribed *by providers* at each visit, however, does not include whether patients had filled prescriptions (i.e. could not measure adherence). Some patients may have a 6-month active prescription for a drug that may not necessarily be refilled at a 3-month follow-up visit. Due to this, we included SLE-specific drug prescriptions as a variable of whether the patient was ever (at any one time point) prescribed (or refilled) a medication throughout the year (2018, 2019, or 2020) as opposed to by visit. We also included codes for infusions for rituximab, belimumab, and cyclophosphamide. We assumed that drug therapies may be an important covariate as some drugs, for instance, mycophenolate mofetil require more frequent laboratory monitoring than others such as hydroxychloroquine. We did not use drug therapy as a surrogate for disease activity.

We also used our covariates to determine any associations with visit types in 2020 when telemedicine was more readily available. We divided patients into either all in-person, two or more telemedicine visits, or in-person with one telemedicine visit to determine if there were differences between the covariates.

#### Statistical analysis

Patient and visit characteristics were summarized by means with standard deviations, median with ranges, or frequencies with percentages. Summary statistics were compared between groups using analysis of variance (ANOVA), independent t-tests, median regression, Wilcoxon rank sum, Fisher's exact, or Chi-square tests according to the type and distribution of each variable of interest. Pairwise tests with Holm's p-value adjustment were done when necessary. Since patients had multiple visits, some comparisons were performed using mixed effects linear regression or

generalized estimating equations (GEEs) to account for the correlated data structure as appropriate. GEE models used an exchangeable correlation structure when possible, otherwise, an independent correlation structure was used. A multiple GEE model was used to determine whether not showing up was associated with visit type appointments. We included covariates that had statistical significanceassociated with no-show or visit type (telemedicine versus in-person). For example, older age and certain medications (methotrexate and belimumab) were more associated with telemedicine visits and introduced into the GEE model. Among patients seen both in 2019 and 2020, GEE was used to determine factors associated with having laboratory test adherence (defined as being performed within 1 month of the visit). For laboratory test visits, the first visit was used if a patient had multiple visits less than 6 weeks apart. The GEE models estimated odds ratios (ORs) with 95% confidence interval (CI). We performed the analysis of "no-shows" on our subgroup of patients that were seen in both 2019 and 2020 to account for the same patients that historically follow-up.

#### **Ethical Considerations**

This study was approved by the Institutional Review Board of the Baylor College of Medicine in affiliation with the Harris Health System. As this was a retrospective review, a waiver of consent was granted. Our data was de-identified and all results were stored in secure and encrypted servers at the Baylor College of Medicine.

#### **Results**

#### Baseline characteristics

Baseline characteristics of included patients are shown in Table 1.

**Table 1. Baseline characteristics of SLE patients** 

	N (%)
Total (N)	156
Gender	
Female	141 (90.4)
Male	15 (9.6)

Race, n=150	
Hispanic	74 (49.3))
Non-Hispanic	35(23.3)
Black	33(23.3)
Non-Hispanic	17 (11.3)
White	
Other	24 (16)
<b>Age,</b> median	43.2 (19.2-
(range)	79.5)
Prescription	
drug use (ever	
prescribed as	
may madian	
per medical	
record)	
-	144 (92 3)
record) Hydroxychloro quine	144 (92.3)
record) Hydroxychloro	
record) Hydroxychloro quine Mycophenolat e	63 (40.4)
record) Hydroxychloro quine Mycophenolat e Azathioprine	63 (40.4) 41 (26.3)
record) Hydroxychloro quine Mycophenolat e Azathioprine Methotrexate	63 (40.4) 41 (26.3) 23 (14.7)
record) Hydroxychloro quine Mycophenolat e Azathioprine Methotrexate Rituximab	63 (40.4) 41 (26.3) 23 (14.7) 4 (2.6)
record) Hydroxychloro quine Mycophenolat e Azathioprine Methotrexate Rituximab Belimumab	63 (40.4) 41 (26.3) 23 (14.7) 4 (2.6) 16 (10.3)
record) Hydroxychloro quine Mycophenolat e Azathioprine Methotrexate Rituximab Belimumab Tacrolimus	63 (40.4) 41 (26.3) 23 (14.7) 4 (2.6) 16 (10.3) 8 (5.1)
record) Hydroxychloro quine Mycophenolat e Azathioprine Methotrexate Rituximab Belimumab Tacrolimus Prednisone	63 (40.4) 41 (26.3) 23 (14.7) 4 (2.6) 16 (10.3)
record) Hydroxychloro quine Mycophenolat e Azathioprine Methotrexate Rituximab Belimumab Tacrolimus	63 (40.4) 41 (26.3) 23 (14.7) 4 (2.6) 16 (10.3) 8 (5.1)

There were 156 patients included in our analysis. Most patients were female (90.4%), Hispanic (49.3%), had a median age of 43, and had received hydroxychloroquine (92%) or prednisone (77%) throughout the follow-up period. Baseline characteristics broken down by visit type are shown in Supplementary Table A1. We included 771 in-person visits and 182 telemedicine (including telephone or video) visits in our analysis. We found that telemedicine visits were associated with older age (median 45.3 vs 41.2 years, p=0.012), and were less likely to occur in patients who were prescribed mycophenolate (40.7% vs 47.6%, p=0.029) or prednisone (78.0% vs 83.5%. p=0.024) compared to in-person visits. Differences in all other characteristics were not statistically significant (Supplementary Table A1b).

Patient characteristics associated with visit type

We determined differences in patient characteristics between those who had all in-person, two

or more telemedicine, or an in-person and one telemedicine visit appointments in 2020 (Table 2).

Table 2. Patient characteristics associated with visit types in 2020

	All in- person (N=21)	Two or more telemedicin e <sup>1</sup> (N=63)	In-person + one telemedicine (N=54)	P-value <sup>2</sup>	Significant pairwise comparison results <sup>3</sup>
Age (first 2020 visit),	36.7 (20.4-	45.1 (20.6-	45.2 (19.8-	0.246	N/A
median (range)	59.9)	77.0)	81.5)		
Gender					
Female	19 (90.5)	59 (93.7)	49 (90.7)	0.759	
Race	n=20	n=61	n=51	0.079	
Hispanic	6 (30.0)	32 (52.5)	25 (49.0)		
Black NH	9 (45.0)	13 (21.3)	11 (21.6)		
White NH	4 (20.0)	3 (4.9)	5 (9.8)		
Other	1 (5.0)	13 (21.3)	10 (19.6)		
Medications	, ,	, ,			
Hydroxychloroquin	17 (81)	47 (74.6)	44 (81.5)	0.671	
е	, ,				
Mycophenolate	9 (42.9)	15 (23.8)	24 (44.4)	0.045	not significant
Azathioprine	5 (23.8)	11 (17.5)	14 (25.9)	0.522	<u> </u>
Methotrexate	3 (14.3)	3 (4.8)	11 (20.4)	0.024	2 or more telemedicin e vs. inperson + 1 telemedicin e, p=0.034
Rituximab	0 (0)	1 (1.6)	1 (1.9)	>0.99	_
Belimumab	1 (4.8)	3 (4.8)	2 (3.7)	>0.99	
Tacrolimus	0 (0.0)	3 (4.8)	2 (3.7)	0.849	
Prednisone	15 (71.4)	27 (42.9)	37 (68.5)	0.008	2 or more telemedicin e vs. inperson + 1 telemedicin e, p=0.026

NH – Non-hispanic

- 1. This includes patients who have only 1 visit in 2020, and that visit is a telemedicine visit
- 2. Calculated using median regression, Fisher's exact or Chi-square test
- 3. Pairwise Fisher's exact test with Holm's p-value adjustment

Patients who had two or more telemedicine appointments were less likely to be prescribed methotrexate (4.8% vs 20.4%, Holm's adj. p-value = 0.034) or prednisone (42.9% vs. 68.5%, Holm's adj. p-value=0.026) during the year compared to those with in-person or only one telemedicine

appointment. Whether the patient was prescribed mycophenolate was significantly different between visit types (p=0.045), but when performing pairwise comparisons on each visit type category, none of them were significant. No patients had received cyclophosphamide in this study.

#### No-shows for clinic visits

All clinic visits from March to September in 2018 and 2019 were in-person (275 in 2018, 305 in 2019). From March to September of 2020, there were 191 (51.2%) in-person visits and 182 telemedicine visits (48.8%) (Table 3). There was no statistical difference in the no-show rates between in-person visits in 2018, 2019, and 2020 (11.3% vs 12.5% vs 16.2% respectively). In 2020, when telemedicine was implemented, the no-show rate for in-person visits was 16.2% versus 5.5% for telemedicine visits (p = 0.002). We used independent GEEs to determine any characteristics associated with no-shows (supplementary Table A2). After adjusting for age and significant SLE prescription drugs (methotrexate and belimumab) in a multiple GEE, there was a significantly decreased odds of no-shows for telemedicine versus in-person clinic appointments (adj. OR 0.39, 95% CI 0.20-0.77, Supplementary Table A3).

Table 3. Visit characteristics stratified by type of visit

	In-Person (N = 771)	Telephone (N = 157)	Video (N=25)	Telephone or Video (N=182)	Total
<b>Year,</b> <i>N</i> (%)					
by row					
2018	275 (100)	0 (0)	0 (0)	0 (0)	275
2019	305 (100)	0 (0)	0 (0)	0 (0)	305
2020	191 (51.2)	157 (42.1)	25 (6.7)	182 (48.8)	373
No-shows, $N$					
(%)					
2018	31 (11.3)	N/A	N/A	N/A	31 (11.3)
2019	38 (12.5)	N/A	N/A	N/A	38 (12.5)
2020	31 (16.2)	7 (4.5)	3 (12)	10 (5.5)	41 (11)

We also performed a subgroup analysis on patients who were seen at least once in 2019 and in 2020. There were 300 visits in 2019 and 332 visits in 2020. The total no-show rates between 2019

and 2020 were similar (11% versus 10.5%, p=0.85). Among these visits, we also found that telemedicine appointments had a significantly lower odds of no-show compared to in-person appointments (adj OR 0.31, 95% CI 0.14-0.69) when adjusting for those SLE prescription drugs that were significantly different (only rituximab) according to type of visit.

#### Laboratory tests utilization

When comparing laboratory test utilization between 2019 and 2020, the only significant difference was in urinalysis which was more frequently performed for telemedicine visits than in person visits (13.1% versus 2.7%, p<0.001, Table 4). We also compared utilization of laboratory tests between in-person and telemedicine visits in 2020 using GEE. No statistically significant differences were observed. We found that there were no differences in non-adherence to lab testing for all labs, though there was a trend towards significance for anti-dsDNA testing (2.9% non-adherence for in-person versus 8.5% non-adherence for telemedicine, p=0.06, Table 4). We found that urine studies had the highest proportion of non-adherences (11.8% for in-person, 14.4% for telemedicine, p=0.51), though this could be explained by other factors not measured such as end-stage renal disease.

Table 4. Nonadherence to laboratory testing for completed visits in 2019 and 2020

Laboratory studies not completed within 30 days of appointment	<b>Total 2019</b> (N = 257)	<b>Total 2020</b> (N = 289)	p- value¹	In- person 2020 (N = 136)	<b>Telemedici</b> <b>ne 2020</b> (N = 153)	p- value
CBC	7 (2.7)	4 (1.4)	0.275	0 (0)	4 (2.6)	N/A
BMP or CMP	5 (1.9)	7 (2.4)	0.705	2 (1.5)	5 (5.3)	0.334
Urinalysis	7 (2.7)	38 (13.1)	< 0.001	16 (11.8)	22 (14.4)	0.512
Anti-dsDNA	19 (7.4)	17 (5.9)	0.479	4 (2.9)	13 (8.5)	0.055
Complements	9 (3.5)	18 (6.2)	0.148	5 (3.7)	13 (8.5)	0.100

CBC – Complete Blood count, BMP – basic metabolic panel, CMP – comprehensive metabolic panel, UA – urinalysis

1. Calculated using GEE with independent correlation structure

#### **Discussion**

We evaluated adherence to telemedicine visits in the management of patients with SLE, at a publicly funded county hospital serving primarily underserved patients. We also determined whether

there were differences in laboratory utilization between patients who received telemedicine versus in person visits. Our results demonstrate that telemedicine encounters had significantly lower odds of no-shows compared to in-person encounters. We also found that no-show rates were similar for 2019 and 2020 despite the emergence of the COVID-19 pandemic, which could be due to the availability of telemedicine, as no-shows for telemedicine versus in-person in 2020 were significantly lower (5.5% vs 16.2%). Furthermore, to our knowledge this is the first study that showstelemedicine visits do not affect laboratory utilization within 30 days of the clinic visits.

Studies have shown that telemedicine can play a role in in the management of chronic diseases that require frequent clinic visits.[15] Other studies in SLE have shown that telemedicine was utilized as frequently as in-person visits during the initial COVID-19 pandemic, though this is the first study to demonstrate that this occurred in an under-resourced patient population.[16,17] Of note, the widespread use of telemedicine however also raises in patients with severe chronic disease such as SLE. A recently published randomized controlled trial in Hong Kong found that the use of telemedicine in patients with lupus nephritis was associated with more hospitalizations.[18] Our study did not address disease activity, or hospitalization, and further research is needed to assess how the wider spread use of telemedicine may impact these factors.

Our study is consistent with studies in other populations that suggest that telemedicine may provide advantages for underserved populations by decreasing missed appointments. One systematic review of 28 studies reported on the use of telehealth for patients for racial and ethnic minority populations. Results showed that the implementation of telehealth improved access to care, however there were still barriers related to technology needed for telemedicine.[19] A separate study utilizing administrative claims data also examined the use of telemedicine in general patient populations and found that telemedicine was associated with less missed appointments.[20] However, this study did not include patient populations such as SLE that require frequent clinic visits and laboratory studies (at least very three to four months). Although our study suggests that telemedicine may be a strategy

to decrease no-show rate in patients with low SES and SLE, more research is needed to determine how other characteristics (including primary language, digital literacy, and disease activity) influence telemedicine and potentially disease outcomes. Furthermore, telemedicine should now be studied as the COVID-19 pandemic has entered the endemic phase.

The strength of our study includes a large number of SLE patients of low SES in one large hospital system where all clinic appointments and laboratory values are documented. There are several limitations in our study. In our study we had predominance of telephone encounters compared to video visits, albeit this has also been seen in other studies, especially amongst patients of black and Hispanic ethnicity and of low socioeconomic status, which were the majority in this population.[21] The use of video visits may affect no-show rate by presenting technological challenges. Second, our study did not adjust for disease severity according to validated indices as it was retrospective, and it only used prescription drug use as a surrogate for severity. Finally, we were unable to adequately control for insurance type at the time of the scheduled appointment as this information is not updated regularly, however, we do not expect this to change the results as over 85% of patients in the HHS are publicly insured or uninsured.

In conclusion, our study shows that the use of telemedicine during the initial phase of the COVID-19 pandemic was associated with a low rate of no-shows in a population of underserved patients with SLE without impacting laboratory utilization. To our knowledge, this is the first study to demonstrate that in patients with SLE telemedicine is not associated with decreased laboratory screening, which is a critical component to the care of patients with lupus. As such, we believe the results of this study warrant further investigation to determine the clinical impact of telemedicine on SLE in prospective studies as the design of this study was not able to capture important clinical characteristics that may influence telemedicine and clinical outcomes including digital literacy and disease activity.

#### Acknowledgements

There are no acknowledgements.

#### **Data Availability**

The participants of this study did not give written consent for their data to be shared publicly.

#### **Conflicts of Interest**

The authors of this study certify that there are no conflicts of interests.

#### **Author Contributions.**

Sebastian Bruera: Conceptualization, Methodology, Analysis, Writing; Kristen Staggers: Formyal Analysis, Writing; Maria Suarez-Almazor: Conceptualization, Methodology, Writing; Sandeep Agarwal: Conceptualization, Methodology, Analysis, Writing. No artificial intelligence (AI) was used in this study or manuscript.

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# **Supplementary Files**