CONSORT-EHEALTH Checklist V1.6.2 Report  
(based on CONSORT-EHEALTH V1.6), available at [http://tinyurl.com/consort-ehealth-v1-6].

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Health Related Quality of Life Improvements in SLE Derived from a Digital Therapeutic Intervention: A Randomized Controlled Pilot Trial

TITLE

1a-i) Identify the mode of delivery in the title  
"A Randomized Controlled Pilot Trial"
1a-ii) Non-web-based components or important co-interventions in title  
The Digital Therapeutic Intervention does include a tele-health coaching component which is not included in the title but can be if necessary. New title would be "Health Related Quality of Life Improvements in SLE Derived from a Digital Therapeutic plus Tele-Health Coaching Intervention: A Randomized Controlled Pilot Trial"
1a-iii) Primary condition or target group in the title  
"Health Related Quality of Life improvements in SLE Derived from a Digital Therapeutic Intervention: A Randomized Controlled Pilot Trial"

ABSTRACT

1b-i) Key features:functionalities/components of the intervention and comparator in the METHODS section of the ABSTRACT  
"To demonstrate that a digital therapeutic intervention, utilizing a mobile app that allows self-tracking of dietary, environmental, and lifestyle triggers, paired with telehealth coaching, added to usual care, improves quality of life in patients with SLE compared to usual care alone."
1b-ii) Level of human involvement in the METHODS section of the ABSTRACT  
Yes. "To demonstrate that a digital therapeutic intervention, utilizing a mobile app that allows self-tracking of dietary, environmental, and lifestyle triggers, paired with telehealth coaching, added to usual care, improves quality of life in patients with SLE compared to usual care alone."
1b-iii) Open vs. closed, web-based (self-assessment) vs. face-to-face assessments in the METHODS section of the ABSTRACT  
No. Subjects were recruited from multiple sources (online forums, referrals from physicians, referral from friends) making this description cumbersome for abstract.
1b-iv) RESULTS section in abstract must contain use data  
"Fifty patients were randomized (23 control, 27 intervention). Adherence with tracking in app and coaching calls was not included in abstract. It can be added to abstract with the following sentence: "Across all subjects, median adherence with daily tracking in the app exceeded 90% and median adherence with coaching calls exceeded 80%.""
1b-v) CONCLUSIONS/DISCUSSION in abstract for negative trials  
N/A

INTRODUCTION

2a-i) Problem and the type of system/solution  
"Yes. "Systemic lupus erythematosus (SLE or lupus) is a multi-system, complex autoimmune disease of unclear etiology affecting at least 1.5 million Americans and 5 million worldwide." There is no cure for SLE and universally effective treatment is not available." A platform has been developed which combines self-tracking technology, analytics, and telehealth coaching to identify and remove possible dietary, environmental, and lifestyle triggers, with the goal to provide clinically meaningful improvements in symptoms and HRQoL, in those with autoimmune disease. The platform is intended as an adjunct to standard of care.
2a-ii) Scientific background, rationale: What is known about the (type of) system  
No. There is no similar product on the market or that has has been tested to our knowledge. However, the basis for looking at diet and environmental factors in SLE is thoroughly discussed ("...emerging evidence from human and animal studies that these epigenetic processes are influenced by dietary, environmental and lifestyle factors.")

Does your paper address CONSORT subtitle 2b?
IRB approval not mentioned in Introduction but rather under Methods. The study was approved by Western Institutional Review Board (CSR: NCT83426334). 

METHODS

3a) CONSORT: Description of trial design (such as parallel, factorial) including allocation ratio  
Yes. "After screening and enrollment, patients were assigned to either the intervention or control arm via randomized blocks of 3 to 8 individuals using a cryptographic random seed." There was not mention that this was 1:1 randomization but that can be added if necessary.
3b) CONSORT: Important changes to methods after trial commencement (such as eligibility criteria), with reasons  
There were no changes to methods after trial commencement.

3b-i) Bug fixes, Downtimes, Content Changes

4a) CONSORT: Eligibility criteria for participants  
Partially.
4a-i) Computer / Internet literacy  
Computer/internet literacy were not included in the Inclusion Criteria as subjects only needed to use a mobile app. "Inclusion criteria included owning a smartphone..."
4a-ii) Open vs. closed, web-based vs. face-to-face assessments:  
Yes. "Participants were recruited through online lupus and autoimmune forums and direct physician referral." During weekly telehealth coaching sessions..." Participants randomized to the intervention group received an email with instructions on how to download and use the app to first track dietary input..." Participants completed an introductory telephone session..." weekly 20-30 minute telehealth coaching sessions were scheduled for the ensuing 15 weeks.
4a-iii) Information giving during recruitment  
No.
4b) CONSORT: Settings and locations where the data were collected  
Yes.
4b-i) Report if outcomes were (self-)assessed through online questionnaires  
Yes. "The participants were asked to complete these PROMs on a secure website prior to the start of the intervention and at weeks 4, 8, 12, and 16." All surveys were completed via a HIPAA-compliant version of SurveyGizmo.

4b-ii) Report how institutional affiliations are displayed  
There were no institutional affiliations in this study.

5) CONSORT: Describe the interventions for each group with sufficient details to allow replication, including how and when they were actually administered

5-i) Mention names, affiliation, affiliations of the developers, sponsors, and owners  
No authors or evaluators are owners of the software. The standard financial stipend provided to 2 of the authors is disclosed in Conflicts of Interest. "Faiz Khan, MD: Standard financial stipends were provided by Mymee, Inc. No other disclosures. Nora Granville: None declared. Raju Mankani: Standard financial stipends were provided by Mymee, Inc. No other disclosures. Yashwant Chathamally, MD: None declared."

5-ii) Describe the history/development process  
Yes. "The platform was developed over several years with extensive feedback from stakeholders in the autoimmune disease community. This has included discussions with patients, family members, physicians, insurance providers, foundations, patient advocacy groups, pharmaceutical companies, and even potential service providers with experience in the sector, such as contract research organizations."

5-iii) Revisions and updating  
No.
5-iv) Quality assurance methods  
No.
5-v) Ensure replicability by publishing the source code, and/or providing screenshots/screen-capture video, and/or providing flowcharts of the algorithms used  
One photo of a screen shot of the subject-facing app is included.
5-vi) Digital preservation  
https://apps.apple.com/us/app/mymee-inc/id1261068992

5-vii) Access  
Partly. "Participants randomized to the intervention group received an email with instructions on how to download and use the app to first track dietary input." The manuscript does not mention that the app was free to subjects and that they were not paid to participate in the study.
5-viii) Mode of delivery, features/functionality/components of the intervention and comparator, and the theoretical framework

5-ix) Describe use parameters
Partially. "...of taking pictures of all the food and beverages consumed daily..." weekly 20-30 minute telehealth coaching sessions were scheduled for the ensuing 15 weeks.

5-x) Clarify the level of human involvement
Yes. "...weekly 20-30 minute telehealth coaching sessions were scheduled for the ensuing 15 weeks.

5-xi) Report any prompts/reminders used
"Following this initial call, weekly 20-30 minute telehealth coaching sessions were scheduled for the ensuing 15 weeks." It is not explicitly stated that during these coaching calls, the importance of daily app usage was reinforced.

5-xii) Describe any co-interventions (incl. training/support)
Yes. "Participants randomized to the intervention group received an email with instructions on how to download and use the app to first track dietary input." After 3-5 days of familiarizing participants with the app, participants completed an introductory 15-minute telephone session to identify their symptoms and goals of the program, review initial tracking data, and provide further training on tracking of other environmental and lifestyle inputs. "...weekly 20-30 minute telehealth coaching sessions were scheduled for the ensuing 15 weeks.

6a) CONSORT: Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
Yes.

6b) CONSORT: Any changes to trial outcomes after the trial commenced, with reasons
Yes. "Patients randomized to the intervention group were assigned to either the intervention or control arm via randomized blocks of 3 to 8 individuals using a cryptographic random seed." It was determined that a sample size of 50 was sufficient to allow for attrition and still produce the needed power with the remaining participants expected to complete the study.

7b) CONSORT: When applicable, explanation of any interim analyses and stopping guidelines
Partially.

8a) CONSORT: Method used to generate the random allocation sequence
Yes. "Patients were assigned to either the intervention group or control arm via randomized blocks of 3 to 8 individuals using a cryptographic random seed." Partially.

8b) CONSORT: Type of randomisation; details of any restriction (such as blocking and block size)
Yes. "...patients were assigned to either the intervention or control arm via randomized blocks of 3 to 8 individuals using a cryptographic random seed.

9) CONSORT: Method used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Yes. "...patients were assigned to either the intervention or control arm via randomized blocks of 3 to 8 individuals using a cryptographic random seed.

10) CONSORT: Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Yes. "...patients were assigned to either the intervention or control arm via randomized blocks of 3 to 8 individuals using a cryptographic random seed.

11a) CONSORT: Blinding - If done, who was blinded and who wasn’t
This was not a blinded study.

11b) CONSORT: Specify who was blinded, and who wasn’t
"Control group participants continued usual care as recommended by their treating physician(s), were not introduced to the intervention app (or any other sham app) and received no training, coaching, or other study interventions.

11c) CONSORT: Whether participants knew which intervention was the “intervention of interest” and which one was the “comparator”
Yes. "Control group participants continued usual care as recommended by their treating physician(s), were not introduced to the intervention app (or any other sham app) and received no training, coaching, or other study interventions.

12a) CONSORT: Statistical methods used to compare groups for primary and secondary outcomes
Yes. "Control group participants continued usual care as recommended by their treating physician(s), were not introduced to the intervention app (or any other sham app) and received no training, coaching, or other study interventions."

13a) CONSORT: For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
Yes.

13b) CONSORT: For each group, losses and exclusions after randomisation, together with reasons
In total, 50 patients were enrolled, with 47 included in ITT analysis and 34 in PP analysis (Figure 2). "Of the 25 ITT intervention participants, 6 (24%) were lost to follow-up after completing 0 or 1 coaching sessions [1 discontinued inclusion medication after 1 session; 1 voluntarily withdrew after 1 session to care for a sick family member; 4 were lost to follow up after completing 1 (3 participants) or no (1) coaching sessions]. Of the remaining 19, 16 completed at least 10 coaching sessions over 16 weeks (for a completion rate of 84%) and were included in PP analysis.

13b-i) Attrition diagram
Yes. Figure 2 (Participant Flow)

13b-ii) Dates defining the periods of recruitment and follow-up
Partially.

13c) CONSORT: Methods for additional analyses, such as subgroup analyses and adjusted analyses
Yes. "Control group participants continued usual care as recommended by their treating physician(s), were not introduced to the intervention app (or any other sham app) and received no training, coaching, or other study interventions."

13d) CONSORT: For each group, losses and exclusions after randomisation, together with reasons
In total, 50 patients were enrolled, with 47 included in ITT analysis and 34 in PP analysis (Figure 2). "Of the 25 ITT intervention participants, 6 (24%) were lost to follow-up after completing 0 or 1 coaching sessions [1 discontinued inclusion medication after 1 session; 1 voluntarily withdrew after 1 session to care for a sick family member; 4 were lost to follow up after completing 1 (3 participants) or no (1) coaching sessions]. Of the remaining 19, 16 completed at least 10 coaching sessions over 16 weeks (for a completion rate of 84%) and were included in PP analysis.

13d-i) Attrition diagram
Yes. Figure 2 (Participant Flow)

13d-ii) Dates defining the periods of recruitment and follow-up
Partially.

13d-iii) Indicate if critical “secular events” fell into the study period
No. There were no critical secular events that fell into the study period.

13d-iv) CONSORT: Why the trial ended or was stopped (early)
No.

15) CONSORT: A table showing baseline demographic and clinical characteristics for each group
Yes.

15b) CONSORT: Report demographics associated with digital divide issues
Yes. In Table 1.

16a) CONSORT: For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Yes. Table 3 shows tracking and coaching session adherence for the ITT and PP groups. For each participant, tracking adherence was calculated as the number of days (24-hour period) at least 1 observation (e.g., symptom, food, other lifestyle input) was entered into the app, divided by the number of days in the 16-week program (112) to arrive at a percentage of days with tracked data (adherence of 100% indicates that the participant used the app to track ≥ once/day each day of the program). Coaching session adherence was calculated as the number of coaching sessions completed divided by 16 and converted to a percentage (adherence of 100% indicates that the participant completed ≥1 session/week each week of the program). Median, 25th and 75th percentile values for tracking and session adherence were then calculated for the whole group. In addition, the percent of participants achieving 70% or greater tracking and session adherence were reported based on early experience with the platform indicating that this level of engagement correlates with better outcomes.

16b) CONSORT: Should be intent-to-treat
Within the intervention group, significant improvement over baseline was noted for FACIT-F (median of 26.0 at end of study vs 16.0 baseline, P=0.042), LupusQoL-burden to others (25.0 vs 16.7, P=0.020), and LupusQoL-fatigue (62.5 vs 25.0, P=0.007). Within the control group, LupusQoL-burden to others (41.7 vs 20.8, P=0.038), LupusQoL-body image (45.0 vs 35.0, P=0.047), and LupusQoL-fatigue (31.3 vs 25.0, P=0.029) saw improvement over baseline at 16 weeks. Comparing the 2 groups, although the intervention group improved more than the control group in 6 of 11 domains (FACIT-F, BDI-SF-pain, interference, LupusQoL-pain, LupusQoL-emotional health, LupusQoL-body image, and LupusQoL-fatigue), none of these comparisons reached statistical significance (Table 4). No significant improvements were uncovered when the Benjamin-Hochberg adjustment was applied to the significance level to account for multiple comparisons.

17a) CONSORT: For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (as 95% confidence interval)
Yes. Tables 4 and 5.

17a-i) Presentation of process outcomes such as measures of use and intensity of use
Table 3 shows tracking and coaching session adherence for the ITT and PP groups. For each participant, tracking adherence was calculated as the number of days (24-hour period) at least 1 observation (e.g., symptom, food, other lifestyle input) was entered into the app, divided by the number of days in the 16-week protocol (112) to arrive at a percentage of days with tracked data (adherence of 100% indicates that the participant used the app to track ≥ once/day each day of the program). Coaching session adherence was calculated as the number of coaching sessions completed by the participant divided by 16 and converted to a percentage (adherence of 100% indicates that the participant completed 1 session/week each week of the program). Median, 25th and 75th percentile values for tracking and session adherence were then calculated for the whole group. In addition, the percent of participants achieving 70% or greater tracking and session adherence are reported based on early experience with the platform indicating that this level of engagement correlates with better outcomes. And see tables 4 and 5 for clinical outcomes.

17b) CONSORT: For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Yes. Figure 3.

18) CONSORT: Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Yes.

18-i) Subgroup analysis of comparing only users
Yes. All results are presented from ITT and PP groups. See Tables 4 (ITT) and 5 (PP).

18-ii) Include privacy breaches, technical problems
No adverse events attributable to the intervention occurred. Four participants (3 from the control group and 1 from the intervention group) experienced lupus exacerbations requiring pulse steroids within the last 4 weeks of the study. Of note, 1 intervention group participant who experienced a flare requiring pulse steroids did not adhere to dietary and lifestyle modifications suggested by the health coach.

19) CONSORT: All important harms or unintended effects in each group
There were no harms or unintended effects in the groups.

19-i) Include privacy breaches, technical problems
No adverse events attributable to the intervention occurred. Four participants (3 from the control group and 1 from the intervention group) experienced lupus exacerbations requiring pulse steroids within the last 4 weeks of the study. Of note, 1 intervention group participant who experienced a flare requiring pulse steroids did not adhere to dietary and lifestyle modifications suggested by the health coach.

19-ii) Include qualitative feedback from participants or observations from staff/researchers
"This exploratory pilot study has many limitations and the results should be interpreted in this context." Selection bias may have been introduced by heavy recruitment from online lupus and other autoimmune patient websites and therefore the study group may not be representative of the general lupus population. However, the number of patients who seek online medical advice is large, continues to grow and crosses gender, age, and socioeconomic differences. Selection bias may have also been introduced by the requirement of owning a smartphone. Smartphone ownership has become increasingly common across gender, race, education and economic levels, [6], hopefully minimizing this bias. "The attrition rate may speak to the requirements inherent in this type of intervention – namely, that participants need to be motivated and engaged with an aptitude for regular app use and an interest in attending weekly coaching sessions in the future. This attention will be addressed by building a run-in period attribute set to mitigate this issue. That this intervention has shown an 83% completion rate (participating in at least 12 of 16 coaching sessions) in 70 autoimmune patients from a private insurance cohort is reassuring that the program has acceptable usability (internal data)."

DISCUSSION
20) CONSORT: Trial limitations, addressing sources of potential bias, imprecision, multiplicity of analyses
20-i) Typical limitations in health trials
Yes. "This exploratory pilot study has many limitations and the results should be interpreted in this context." Selection bias may have been introduced... "Selection bias may have also been introduced by the requirement of owning a smartphone." There was no sham app or sham coaching in the present study. Digital apps and health coaching alike are intrinsically engaging thus vulnerable to the placebo response. It is not possible to tell to what extent HRQoL improvements were influenced by this engagement and patient expectations rather than the program interventions.

21) CONSORT: Generalisability (external validity, applicability) of the trial findings
21-i) Generalisability to other populations
"Finally, given the expected role of diet, environment and lifestyle on other autoimmune diseases, many of which have gaps in care similar to those in SLE, studies of the intervention’s application to other autoimmune conditions is warranted.

21-ii) Discuss if there were elements in the RCT that would be different in a routine application setting
There are no significant elements of the RCT that differ from routine use of the application. Interaction with the app, coaches and assessment of outcome measures are similar when app is used routinely.

22) CONSORT: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
22-i) Restate study questions and summarize the answers suggested by the data, starting with primary outcomes and process outcomes (use)
"To the authors’ knowledge, this is the first study to show that a digital therapeutic intervention designed to address environmental and lifestyle factors can improve HRQoL when added to usual care in patients with SLE. Participants who completed the 16-week protocol showed continuous improvement across all HRQoL domains and statistically greater improvement than those receiving usual care alone for the majority of domains.

22-ii) Highlight unanswered new questions, suggest future research
"While the above findings do not provide conclusive evidence linking dairy, gluten, nightshades or other foods to SLE, accumulating data from in vitro, animal and human studies suggest potential mechanisms. Further research could be valuable in future studies of this digital therapeutic to assess microbiome composition before and after the intervention.

Other information
23) CONSORT: Registration number and name of trial registry
"ClinicalTrials.gov: NCT010416384RT"

24) CONSORT: Where the full trial protocol can be accessed, if available
The full trial protocol is not currently publicly accessible.

25) CONSORT: Sources of funding and other support (such as supply of drugs), role of funders
"Funding: This study is supported by funds from the sponsor, Mymee,Inc. "Role of Sponsor: The sponsor provided funding for delivery of the intervention, study management, and stipends made to some study team members; managed the participant recruitment process under PI supervision; and delivered the intervention protocol to intervention participants.

X26-i) Comment on ethics committee approval
No

x26-ii) Outline informed consent procedures
No. The informed consent form can be included in submission if desired.

X26-ii) Safety and security procedures
No

X27-i) State the relation of the study team towards the system being evaluated
"Conflicts of Interest
Faiz Khan, MD: Standard financial stipends were provided by Mymee, Inc. No other disclosures. Nora Granville: None declared.

Raja Malkani: Standard financial stipends were provided by Mymee, Inc. No other disclosures.

Yashwant Chathampally, MD: None declared."