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TITLE: A Walking Intervention to Improve Fatigue and Quality of Life in Lupus: A Randomized, Controlled Trial

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CONTRACTING ORGANIZATION: University of California San Francisco

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14. ABSTRACT The objective of this project is to implement a simple pedometer-based walking intervention to improve fatigue and quality of life for individuals with lupus. The project addresses two aims: (1) Test the impact of the intervention on activity levels of persons with systemic lupus erythematosus (SLE) using a randomized controlled trial design; and (2) Test the impact of the intervention on fatigue levels and other domains of quality of life, including physical functioning, pain interference, depressive symptoms, cognitive symptoms, social functioning, and sleep disturbance. To date, we have achieved the first two major tasks from the SOW projected to be completed in the first 6 months of the project: IRB approval from both the local IRBs and HRPO, and development of the protocol, including interview protocol, manual of operations, all patient-facing materials, and construction of database for participant screening, tracking, and entry of data. We have made substantial progress in recruiting participants, having reached 50% accrual as of the end of project year 2.					
15. SUBJECT TERMS Lupus, fatigue, quality of life, physical activity					
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1. INTRODUCTION

The objective of this project is to implement a simple pedometer-based walking intervention to improve fatigue and quality of life for individuals with lupus. The project addresses two aims: (1) Test the impact of the intervention on activity levels of persons with systemic lupus erythematosus (SLE) using a randomized controlled trial design; and (2) Test the impact of the intervention on fatigue levels and other domains of quality of life, including physical functioning, pain interference, depressive symptoms, cognitive symptoms, social functioning, and sleep disturbance.

We will test the effect of a walking intervention on increasing physical activity and decreasing fatigue, as well as improving other aspects of quality of life. After objective assessments of physical activity at baseline, participants will be randomized to one of two groups (n = 57 in each group): an intervention group that will receive a pedometer/activity monitor plus individualized step targets or a wait-list control group. Both groups will be followed over 21 weeks with the same measurements and contacts. At the end of the 21-week period, the wait-list control group will begin the intervention. The intervention group will have a follow-up 4 months after the end of the intervention to assess maintenance of activity, fatigue, and other quality of life domains.

2. KEYWORDS:

Lupus, physical activity, fatigue, quality of life

3. ACCOMPLISHMENTS

What were the major goals of the project?

Major task 1: IRB approval

	Target date	Completion
Local IRB approval	Month 3 (Oct 2021)	COMPLETED Nov 1 2021
HRPO approval	Month 6 (Dec 2022)	Submitted to HRPO Nov 2021; COMPLETED Feb 2022

Major task 2: Protocol development

	Target date	Completion
Questionnaire, study visit protocol, manual of operations, patient-facing materials completed	Month 3 (Oct 2021)	COMPLETED.
Database for participant screening, tracking, and data entry	Month 4 (Nov 2021)	COMPLETED. May 2022. We were a few months later than the projected completion date because we opted to incorporate all study activities into a REDCap database for better tracking and integration.
Study ready to recruit participants	Month 6 (Jan 2022)	COMPLETED. All programming and testing were completed in June 2022

Major task 3: Baseline study visits

	Target date	Completion
Baseline visits begin	Month 6 (Jan 2022)	Began recruitment and scheduling in May 2022. First participant seen in June 2022
Complete 55 baseline visits	Month 18 (Jan 2023)	COMPLETED, June 2023.
Complete 114 baseline visits	Month 30 (Jan 2024)	In process.

Major task 4: Final study visits for initial intervention group

	Target date	Completion
Follow-up visits begin	Month 18 (Jan 2023)	Follow-up visits have proceeded as originally projected with those who have been enrolled.
Follow-up visits completed	Month 34 (May 2024)	

Major task 5: Intervention implemented for waitlist controls

	Target date	Completion
Intervention visits begin for waitlist controls	Month 11 (July 2022)	In process.
Final intervention visits for waitlist control group	Month 39 (Oct 2024)	

Major task 6: Extended follow-up for initial intervention group

	Target date	Completion
Extended follow-ups begin	Month 15 (Oct 2022)	In process.
Extended follow-ups completed	Month 42 (Jan 2025)	

Major task 7: Quality control and data cleaning

	Target date	Completion
Quality control checks during data entry	Months 6-42 (Jan 2022 – Jan 2025)	Data cleaning occurs on an ongoing basis. In addition, quality control checks are programmed into the REDCap database.
Data cleaning	Months 8 – 42 (Mar 2022 – Jan 2025)	

Major task 8: Data analysis and manuscript preparation

	Target date	Completion
Analysis and manuscript preparation	Months 40-46 (Nov 2024 – May 2025)	
Manuscript of primary results prepared and submitted	Month 46 (May 2025)	
Additional manuscript(s) prepared and submitted	Month 48 (July 2025)	

What was accomplished under these goals?

Major task 1, IRB approval: COMPLETED

- We obtained local IRB approvals from both UCSF and CPMCRI, as well as HRPO approval.

Major task 2, Protocol development: COMPLETED

The following tasks were completed:

- Development of the study REDCap database, which included programming and testing of:
 - The screening questionnaire and protocol
 - Scheduling of visits and contacts
 - Interview protocols for baseline, mid-point, and final assessment
 - Scheduling of check-ins
 - Entry of initial week actigraph monitoring and calculation of step targets for each two-week period
 - Entry of lab values
- Development and testing of actigraph protocol and sleep/wake diary.
- Integrating a randomization protocol within REDCap.
- Development and testing of protocol for syncing participant Fitbit data so that the study can retrieve daily step information.
- Development and testing of participant-facing instruction manuals for use and syncing of Fitbits.
- Development of step diaries for participants who either do not have smart phone access to sync their Fitbits or who prefer to use the diary.

- Establishment and testing of Quest Lab account for processing of blood samples.
- Development of recruitment materials, including study brochures in English and Spanish.
- Development of study Manual of Operations.
- Training of study staff to conduct all study procedures.
- Translation of all patient-facing materials (recruitment, interviews, etc.) to Spanish

Major task 3, Baseline study visits: Ongoing

- Recruitment began in May 2022, and the first baseline visit took place in June 2022.
- While we are behind the original timeline originally proposed, we feel that the additional set-up time will benefit the project in the long run through improved integration of study components, better capabilities for tracking participants, integrated randomization, better data quality control, and easier transition from the database to analyzable datasets.
- We have a pool of individuals who have participated in previous studies who are our primary recruitment focus at this time.
- To date, all participants have agreed to come to in-person visits which allows us to conduct blood draws and explain all study procedures (such as use of the Fitbit and syncing with smart phones) in-person. Based on our experience in our previous lupus sleep study, we had expected that participants would still be wary of in-person visits, so we also devised study protocols to allow for remote visits. However, we structured the study incentives to encourage the in-person visits, offering a larger amounts for in-person than for remote visits.
- To date, all participants have been English-speaking. The intent was to ensure that all study procedures were working well before extending to Spanish-speakers. Now that we have enrolled several participants, we will expand recruitment to Spanish-speaking patients in September 2022.
- Overall, the study is progressing nicely. Recruitment is ongoing successfully, procedures are operating smoothly, and we have an excellent staff.

• Enrollment through June 2023

As reported in the previous annual report, we had a 6-month delay in recruitment. In the past year, however, we have geared up and are experiencing success in recruiting, having reached 50% accrual of our projected total at the end of June 2023. We had projected a 93% retention to final follow-up, leaving a sample of 107 for complete analysis. To date, we have had only 2 withdrawals. Six participants (three from the intervention group with four-month long-term follow-up; three from the waitlist control group) have completed the study.

	Year 1 (Jul 2021 – Jun 2022)				Year 2 (Jul 2022-Jun 2023)				Year 3 (Jul 2023 – Jun 2023)				Total
	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	
Recruitment projected in application			15	15	15	15	15	15	15	15			115
Actual recruitment (through Jun 2023)				1	8	8	22	18					57

Major task 7: Quality control and data cleaning

- Quality control is an integral part of our procedures. For example, the RedCAP data entry fields are programmed not to allow out of range responses, responses are from drop-down menus when possible to limit response options, and calculations (e.g., for step targets) are hard-coded rather than being calculated individually by study personnel. We examine reports of study progress regularly.

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

• During the next reporting period, we will continue recruitment and implementation of the intervention. We anticipate that enrollment will be completed by the end of Year 3.

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

• There were no changes in the overall design of the project.

• In addition to the primary study procedures using in-person visits, we developed protocols to allow for remote participation. This was done based on our experience with our just-completed lupus study, which was begun during the COVID-19 pandemic. In that study, participants were reluctant to attend in-person research study visits, so we pivoted to a completely remote study. We used that experience to inform the remote study protocol for the current intervention. However, we are providing additional incentives for in-person visits, so we hope that participants will be more amenable to coming into the study site. So far, all baseline visits have been in-person.

• Dr. Sarah Patterson, co-investigator, has an interest in the molecular basis behind the effects of lifestyle interventions in rheumatic diseases. Of particular interest, she recently published a study showing that individuals with rheumatoid arthritis (RA) who were more physically active had lower expression of immune signaling pathways implicated in RA pathogenesis (Patterson SL et al. Physical activity associates with lower systemic inflammatory gene expression in rheumatoid arthritis. *J Rheumatology* 2022; 49:1320-1327. doi: 10.3899/jrheum.220050).

Based on her interest and supported by other funds, we have begun collecting RNA samples at the beginning and end of the intervention to allow a future analysis of molecular changes that may occur following participation in our intervention. This future analysis has the potential to add an important and novel dimension to our study.

Actual or anticipated problems or delays and actions or plans to resolve them

• The major change in our approach was the decision to administer the entire study through REDCap, as described above. While this delayed the beginning of recruitment and enrollment somewhat, we believe that the advantages will benefit the project and enhance its long-term success.

• No new problems or delays in the previous year.

Changes that had a significant impact on expenditures

• Due to the delay in beginning enrollment, our expenditures for participant reimbursements and laboratory costs are delayed.

• The subcontract expenditures from Dr. Stone's lab have also been delayed due to overall delays in the project as described above. Those expenditures will be charged to the project as the work progresses.

• Dr. Patterson received a career development award (K award from NIH) and can no longer take salary from the project. However, she remains actively involved, and her role as originally described has not changed.

• No changes in the previous year.

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use of vertebrate animals

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

6. PRODUCTS**Publications, conference papers, and presentations**

Nothing to report

Website(s) or other internet site(s)

Nothing to report

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other products

Nothing to report

7. PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Patricia Katz
Project Role:	PI
Research identifier (e.g., ORCID ID)	ORCID 0000-0002-8146-2519
Nearest person month worked:	1.2
Contribution to the project	Overall project direction, supervision of all project activities, liaison with funder

Name:	Sarah Patterson
Project Role:	Co-investigator, UCSF
Research identifier (e.g., ORCID ID)	ORCID 0000-0002-6661-019X
Nearest person month worked:	2.4
Contribution to the project	Clinical expertise in lupus

Name:	Jing Cheng
Project Role:	Co-investigator, UCSF
Research identifier (e.g., ORCID ID)	ORCID 0000-0002-0417-3713
Nearest person month worked:	0.6
Contribution to the project	Biostatistical support

Name:	Jennifer Niemi
Project Role:	Senior Clinical Research Coordinator
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	8.4
Contribution to the project	Recruitment and screening of study participants; conduct study visits, interviews, and check-in contacts; train all other research assistants on study procedures

Name:	Joonsuk Park
Project Role:	Clinical Research Coordinator
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	2.6
Contribution to the project	Development and maintenance of RedCAP data entry program; developing and managing RedCAP reports; assisting as needed with vendors (e.g., outside laboratory) and other administrative functions

Name:	Jie Yu (Emmy) Li
Project Role:	Clinical Research Coordinator
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	2.4
Contribution to the project	Recruitment and screening of study participants; conduct study visits, interviews, and check-in contacts

Name:	Miriam Katz
Project Role:	Clinical Research Coordinator
Research identifier (e.g., ORCID ID)	3.6
Nearest person month worked:	
Contribution to the project	Recruitment and screening of study participants; conduct study visits, interviews, and check-in contacts

Name:	José Pinzón Tirado
Project Role:	Research assistant

Research identifier (e.g., ORCID ID)	
Nearest person month worked:	7.2
Contribution to the project	Recruitment and screening of study participants; conduct study visits, interviews, and check-in contacts

Name:	Stephanie Rush
Project Role:	Database manager
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	1.8
Contribution to the project	Design, development and maintenance of REDCap database.

Name:	Katie L. Stone
Project Role:	Co-investigator, California Pacific Medical Center Research Institute (CPMCRI)
Research identifier (e.g., ORCID ID)	ORCID 0000-0003-2797-3171
Nearest person month worked:	0.46
Contribution to the project	Overall project direction and supervision of all project activities with regard to actigraph assessments, scientific liaison with UCSF team

Name:	Katherine Peters
Project Role:	Biostatistician, CPMCRI
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	0.36
Contribution to the project	Developing scoring protocols for actigraph data, including data transfer

Name:	Vicki Li
Project Role:	Project assistant, CPMCRI
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	0.36
Contribution to the project	Reviewing, cleaning, and scoring actigraphy files

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

P. Katz

Reductions total = 26%

- Genentech Health Equity Innovations Grant: effort reduced from 1% to 0
- Rheumatology Research Foundation (Development and preliminary validation of a patient-reported measure of systemic lupus erythematosus disease activity, PI: Katz). Effort reduced from 20% to 10%.
- U01DP006486 (Racial/ethnic and socioeconomic disparities in biologic and clinical SLE outcomes. Co-PIs: Dall'Era, Yazdany). Grant ended. Effort reduced from 15% to 0.

Additions total = 25%

- U48DP006374-03-03 (The impact of psychological factors on patient-reported outcomes among individuals with lupus, PI: Katz): Previously listed as pending. Now funded, 10% effort
- U01DP006701 (Racial/ethnic and socioeconomic disparities in biologic and clinical SLE outcomes [renewal]. Co-PIs: Dall'Era, Yazdany, Katz). Now funded, 15% effort

What other organizations were involved as partners?

Organization Name:	California Pacific Medical Center Research Institute (CPMCRI)
Location of Organization:	San Francisco, CA
Partner's contribution to the project	Collaboration. Dr. Katie Stone's lab at CPMCRI is providing expertise in the collection and scoring of actigraph measurement of activity.

8. SPECIAL REPORTING REQUIREMENTS

Nothing to report

9. APPENDICES

Nothing to report