AWARD NUMBER: W81XWH-21-1-0457

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

PRINCIPAL INVESTIGATOR: Patricia Katz

CONTRACTING ORGANIZATION: University of California, San Francisco, CA

REPORT DATE: August 2022

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
August 2022	Annual	01Aug2021-31Jul2022

4. TITLE AND SUBTITLE

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

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-21-1-0457

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Patricia Katz

E-Mail: patti.katz@ucsf.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

REGENTS OF THE UNIVERSITY OF CALIFORNIA
1855 FOLSOM ST STE 425
SAN FRANCISCO CA 94143-4249

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

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 begun to recruit participants and have conducted 4 baseline assessments.

15. SUBJECT TERMS
Lupus, fatigue, quality of life, physical activity

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	11	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

Page

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, sleep, stress, trauma, disease activity

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)	
Complete 114 baseline visits	Month 30 (Jan 2024)	

Major task 4: Final study visits for initial intervention group

	Target date	Completion
Follow-up visits begin	Month 18 (Jan 2023)	
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)	We anticipate these will begin in November 2022.
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)	We anticipate these will begin in March 2023.
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 Fitibt 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.

Major task 7: Quality control and data cleaning
• Quality control is an integral part of the REDCap database. For example, 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.

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 enrollment and administering the intervention.

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.

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.

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.

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:	0.6
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:	Research assistant
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	4.9
Contribution to the project	Development and testing of study interview protocol, recruitment and screening of study participants, conduct study visits, train all other research assistants on study procedures

Name:	Joonsuk Park
Project Role:	Research assistant
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	4.0
Contribution to the project	Development and testing of study interview protocol, assist in development and maintenance of RedCAP data entry program,

Name:	Ishani Deshpande
Project Role:	Research assistant
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	1.7
Contribution to the project	Development and testing of study interview protocol, recruitment and screening of study participants

Name:	Miriam Katz
Project Role:	Research assistant
Research identifier (e.g., ORCID ID)	0.8
Nearest person month worked:	
Contribution to the project	Development and testing of study interview protocol

Name:	José Pinzón Tirado
Project Role:	Research assistant
Research identifier (e.g., ORCID ID)	

Nearest person month worked:	0.9
Contribution to the project	Development and testing of study interview protocol, translation of all materials to Spanish, recruitment and screening of study participants and conduct of study visits for Spanish-speaking participants

Name:	Stephanie Rush
Project Role:	Database manager
Research identifier (e.g., ORCID ID)	
Nearest person month worked:	1.5
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?
Nothing to report

P. Katz
Reductions total =37%
• Genentech Health Equity Innovations Grant: effort reduced from 5% to 1%

• NIAMS R01 AR072040 (Sleep disturbance in rheumatoid arthritis, PI, Katz): effort reduced from 20% to 0. (grant now in no-cost extension)

• NHLBI R01 HL134851 (Frailty and patient-centered outcomes in candidates for lung transplantation, PI: Singer): effort reduced from 10% to 0. Grant has ended.

• R18 HS025638 (Rheumatology Informatics System for Effectiveness Patient-Reported outcome Dissemination Project, PI: Yazdany): effort reduced from 3% to 0. Grant has ended.

Additions total = 35%
• 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

• Rheumatology Research Foundation (Development and preliminary validation of a patient-reported measure of systemic lupus erythematosus disease activity, PI: Katz). New funding beginning July 1, 2022, 20% effort.

• U19HL145435 (The California Labor Laboratory Total Worker Health Center of Excellence, PI: Yelin): New funding beginning July 1, 2022, 5% effort.

S. Patterson
• K23HL138461 (Career development award): New funding, beginning January 2022. Dr. Patterson is no longer able to take funding from this DoD award, but is contributing time. The focus of the DoD project is consistent with the overall goals of her K award.

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