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TITLE: Validating Community-Based Measures of Activity in Ambulatory Duchenne Muscular Dystrophy

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5d. PROJECT NUMBER

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

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12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This research project will validate use of patient generated step and activity data for data collection at the point-of-care to support use of stride rate patterns as an outcome measure for ambulatory patients with DMD. We will include step activity monitoring by laboratory and consumer level step monitoring devices that can feed data through
Apple HealthKit into the UC Davis instance of the Epic electronic medical record system. Up to 60 ambulatory patients with DMD will be recruited to represent the early, middle and late stages of the progressive loss of ambulation in DMD. Up to 150 control patients will be recruited and split into similar age ranges. Participants will be assessed using step monitoring devices and traditionally performed clinical outcome measures, followed by community monitoring. StepWatchTM data collected from two previously enrolled cohorts of children with DMD will also be used for longitudinal analyses and determination of responsiveness to steroid treatment.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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Unclassified	Unclassified	Unclassified	Unclassified		USAMRMC

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1. INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Background: Development of novel technologies and therapeutic agents to treat Duchenne muscular dystrophy (DMD) have increased interest by regulatory bodies such as the Food and Drug Administration in the development of "clinically-meaningful" study endpoints for clinical trials. There is a need for the development of valid measures of ambulatory ability in very young children while effectively evaluating treatment effects in clinical trials.

Objective: This proposal focuses on validating the use of patient generated step and activity data to facilitate future data collection at the point-of-care to support the development of stride rate patterns as an outcome measure for ambulatory patients with DMD. It is to include step activity monitoring by StepWatch™ and a consumer level step monitoring devices (Garmin VivoActiveHR and Polar M400 activity watches and the Polar StrideSensor activity monitor) that can feed data through Apple HealthKit into the UC Davis instance of the Epic electronic medical record system. Up to 60 ambulatory patients with DMD will be recruited to represent the early, middle and late stages of the progressive loss of ambulation in DMD. Patients will be sorted into three age groups of (n=20) participants: early (ages 2-6), middle (ages 7-11) and late (ages 12-16). Up to 150 control participants will be recruited and split into similar age ranges. Participants will be assessed using step monitoring devices and traditionally performed clinical outcome mesures (6MWT, TFTs, NSAA), followed by community monitoring. StepWatch™ data collected from two previously enrolled cohorts of children with DMD will also be used for longitudinal analyses and determination of responsiveness to steroid treatment. We will develop model plans for data collection, validation, visualization, transfer, archival and lock of raw instrument data, as well as guidelines for integration with existing data platforms including EPIC electronic health records and I2B2 NIH data repository.

Applicability: Well-designed community mobility measures can be used in both clinical trials and day-to-day clinical practice. For clinical trials, they provide researchers with the ability to measure day-to-day walking ability across a broad range of ages, including very young children with DMD. Those results can then also be compared to other clinical trial measures such functional evaluations and timed function tests to help teach researchers and regulatory authorities about how "in clinic" tests commonly used in clinical trials relate to a persons' mobility in their daily life and whether those tests are "clinically meaningful". Within 3 years, this project will be able to produce such a tool.

Impact and Contributions: Data from this project will provide the basis for development of a "clinical trialready" community mobility measure that has been constructed against a background of comprehensive clinical assessments of functional ability across the range of ambulatory ability. This measure will be rapidly usable as a sensitive measure for use in the growing field of DMD clinical trials, and will help to demonstrate "clinically meaningful" results to regulatory agencies in charge of new drug approval.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Duchenne muscular dystrophy
Community Mobility
mHealth
Patient Generated Health Data
Accelerometers
Clinical Trial Outcomes Development
DMD Natural History

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Aim 1: Comparison of accuracy and validity of both laboratory- and consumer-grade step activity monitoring devices, and comparison to traditional clinical evaluator determined laboratory-based measures.

- Aim 1.1: Evaluate validity and correlation of stride activity data using laboratory and consumer grade devices.
- Aim 1.2: Determine concurrent validity of stride rate patterns by accelerometry as compared to the 6-minute walk test, North Star Ambulatory Assessment and Timed Motor Performance Tests in DMD patients who are able to perform these assessments.

Aim 2: Evaluation of age-related patterns in community step monitoring data in DMD and typically developing youth controls.

- Aim 2.1 Evaluate differences between DMD and TDY in overall daily patterns of activity by age group
- across all levels of stride rate activity.
- Aim 2.2 Evaluate differences between DMD and TDY for area under the curve for total time and height-adjusted distance overall and at each stride rate and stride activity level group.
- Aim 2.3 Evaluate Differences between age groups that represent disease progression in DMD for area under the curve for total time and height-adjusted distance overall and at each stride rate and stride activity levelgroup.

Aim 3: Evaluation of historical community stride monitoring data from natural history studies and clinical trials to evaluate longitudinal change and steroid response characteristics.

- Aim 3.1 Evaluate longitudinal rate of change characteristics of stride activity monitoring in DMD using
- historical natural history data.
- Aim 3.2 Evaluate longitudinal rate of change characteristics of stride activity monitoring to identify
- differences due to glucocorticoid therapy using historical clinical trial data.

Aim 4: We will develop, evaluate and provide recommendations for a framework to collect, and track patient generated health data in the electronic health record for clinical care and to transfer this data into a database to meet Federal 21CFR11 compliance for clinical research.

- **Aim 4.1:** Develop guidelines for developing a platform to collect PGHD, guidelines for storage,
- visualization and providing clinical care in the EPIC electronic health record.
- **Aim 4.2:** Provide guidelines for the transfer of de-identified patient-generated health data (PGHD) collected via this methodology to meet FDA 21CFR11 compliance. In addition develop guidelines for sharing deidentified PGHD using a platform like the I2B2 NIH data repository for clinical research.

What was accomplished under these goals?

Aim 1: Comparison of accuracy and validity of both laboratory- and consumer-grade step activity monitoring devices, and comparison to traditional clinical evaluator determined laboratory-based measures.

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- Aim 1.2: Determine concurrent validity of stride rate patterns by accelerometry as compared to the 6-minute walk test, North Star Ambulatory Assessment and Timed Motor Performance Tests in DMD patients who are able to perform these assessments.

Accomplishments and Results: An initial set of equipment was procured for this project and includes the new StepWatch 4 device, which is considered the ”gold standard” for community monitoring in DMD as well as commercial monitors by Garmin and Polar. After a delay in receiving the SW4, our clinical evaluator created CRF forms for data collection that were included in the initial application to the UC Davis IRB. Our initial application and protocol to begin data collection is with the UC Davis IRB for review. Once we have approval from UC Davis and DoD, we will begin subject recruitment and data collection.

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- Aim 2.1 Evaluate differences between DMD and TDY in overall daily patterns of activity by age group
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Accomplishments and Results: UC Davis rolled out an upgraded version of the EPIC medical record. This newly upgraded system will impact our development of guidelines and recommendations for Aim 4. Dr. Dharmar has been an integral part of this upgrade at the medical center and will be developing his recommendations based on this experience.

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

Nothing to Report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report

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

Nothing to Report

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

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:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Due to the rapidly developing of commercial monitoring devices, we will be exploring the inclusion of the Apple Watch in this project. Our initial inclusion of iPhones for each participant may not represent the most current technology for monitoring stride in the community. Also, most participants will already have access to a SmartPhone and can use their own devices as needed.

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

The delay in the release of the Step-Watch 4 affected the development of our research protocol. In addition, the release of newer versions of the Apple Watch has led to a possible change in commercially available equipment for data collection. Once the current protocol is approved, we will complete a small pilot for each device to determine if there are any limitations or changes necessary for data collection.

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

Publications, conference papers, and presentations

Nothing to Report

Journal publications

Nothing to Report

Books or other non-periodical, one-time publications.

Nothing to Report

Other 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 & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Craig McDonald, MD (PI) - No Change
Name: Erik Henricson, MPH (Co-Investigator) - No Change
Name: Madan Dharmar, PhD (Co-Investigator) - No Change
Name: Alina Nicorici, BS (Clinical Evaluator) - No Change
Name: Corey Owens, MS (Data Manager) – No Change

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

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.