ARIC Manuscript Proposal #4134

PC Reviewed: 10/11/22	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Definition and Validation of Activity Cut Points for the Zio XT Patch Accelerometer

b. Abbreviated Title (Length 26 characters): Activity Cut Points for Zio XT

2. Writing Group:
Lacey Etzkorn, Jennifer Schrack, Lin Yee Chen, Amal Wanigatunga, Ciprian Crainiceanu, Francesca Marino, Erin Dooley, Kelley Gabriel, Anis Davoudi, Hau Tieng-Wu. *Please note this is not the intended ordering of authors for publications. Ordering will be decided prior to submission. Other authors are welcome.

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. **__LE__ [please confirm with your initials electronically or in writing]**

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3. Timeline:
Accelerometry data (Visit 6 as part of the Zio XT and Physical Activity and Falls ancillary studies) are already collected and will be made available to the analyst/primary author by Kelley Gabriel and Lin Yee Chen through Jennifer Schrack.
Statistical Analysis: 4 months (December 2022)
Manuscript Preparation: 4 months (April 2023)

4. Rationale:

Wearable accelerometers are devices which measure movement and are widely used in health studies to estimate physical activity (PA). In an analysis of ARIC data, Davoudi et al

demonstrated that the Zio XT (iRhythm Technologies Inc, San Francisco, CA, USA), an ambulatory electrocardiogram which also contains an accelerometer, produced useful measures of PA, which were highly correlated with PA measures from another validated accelerometer, the Actigraph GT3X (ActiGraph LLC, Pensacola, FL, USA) [1]. In an analysis of Zio data from the Multicenter AIDS Cohort Study, Zio PA summaries had expected associations with several clinical factors (i.e. lower day-time PA was associated with higher weight, slower gait, needing a mobility assistance device, older age, using tobacco, HIV infection, worse depression symptoms, lower eGFR, worse lipid measurements, and diabetes status) [2].

Methods for quantifying human movement with the onboard Zio accelerometer have not been fully developed. Processing of accelerometer data for health research requires summarizing a high-dimensional, multivariate timeseries into a few meaningful summary variables to be used in further analysis. For example, summaries commonly used with the GT3X include total activity counts (TAC), which conveys the wearer's total amount of daily PA[3]. However, many health researchers are unfamiliar with the units and typical distributions of counts, so results can be unintuitive. Another common technique for quantifying PA is to summarize the daily minutes a participant spends at various activity levels (i.e. sedentary, light, moderate, and vigorous intensity PA) [4]. Since these summaries have units of daily minutes, they are often more intuitive for health researchers.

However, daily time spent performing sedentary, light, and moderate or vigorous intensity PA cannot yet be quantified with Zio as this method requires the development of cut points (i.e. the measurement of activity intensity which demarcates two adjacent activity categories). Accelerometer cut points for Zio XT cannot be borrowed directly from previous work because the magnitude and distribution of activity measurements can vary by the model of accelerometer, the placement of the accelerometer, the method used to quantify intensity of movement, and the population to which they are applied. For example, previous work in ARIC used cut points designed for the Actigraph GT3X mounted at the waist among older adults when activity intensity is quantified using minute-level vector magnitude activity counts [5,6]. In contrast, Zio is mounted on the chest and contains a different model of accelerometer, and previous studies utilizing Zio Accelerometry quantified PA using mean absolute deviation (MAD) instead of vector magnitude counts [1,2]. To bridge this research gap, we propose to create cut points for Zio using ARIC participants who wore Zio and the GT3X simultaneously during visit six ($N > 250$). These data will allow us to characterize the association between Zio and ActiGraph measurements of activity intensity, and to appropriately map cut points from the latter device to the former. The creation of Zio cut points will aid ARIC researchers who want to understand associations between health outcomes and daily time spent at various levels of activity intensity.

5. Main Hypothesis/Study Questions:

Our goal is to create and validate PA intensity cut points for use with Zio XT accelerometer data. Using both Zio and the GT3X, we will characterize the participants' daily amount of time spent performing light and moderate-to-vigorous intensity PA (LIPA and MVPA), and we will demonstrate that LIPA and MVPA measurements produced by Zio are highly correlated with those measurements from the GT3X.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

2.1 ARIC Sample, PA Assessment. In 2015-16, more than 250 ARIC participants wore the Zio XT and ActiGraph GT3X simultaneously for up to seven days [1]. As in Dooley et al. [5], we will screen the GT3X data for non-wear using the Choi algorithm [7] and summarize minute-level PA from the GT3X data as vector magnitude counts (VMC), the proprietary activity summary metric for ActiGraph. We will screen the Zio acceleromter data for non-wear using the algorithm proposed by Etzkorn et al. [8], and we will summarize minute-level PA as mean absolute deviation (MAD) as in Davoudi et al. [1]. For all analyses, we will retain only data from periods during which both devices were worn.

2.2 Statistical Analysis. First, we will construct functions that defines the relationship between VMC from the GT3X and MAD from Zio. These functions will be constructed via two distinct approaches to increase robustness.

For the first approach, we construct a two-sample quantile-quantile function by pooling minute-level MAD and VMC measurements from across all participants and all wear time. In a two-sample quantile-quantile function, repeated measurements of two random variables (MAD and VMC) are sorted into order statistics, and the *i*th order statistic from the distribution of MAD is paired with the *i*th order statistic from the distribution of VMC. An interpolation can be drawn between the points on this graph, and the result is a monotonic, increasing function. (See Tsai [9] for further description of quantile-quantile functions.)

For the second approach, we will use penalized splines to regress Zio MAD on concurrent GT3X VMC as in Karas et al. [10]. If discrepancies exist, the fit and assumptions underlying each method will be compared, and a preferred method will be selected. We will examine whether the mapping functions from both approaches vary by age, gender, height, weight, and BMI. If mapping functions vary by these characteristics, we will continue with stratified mapping functions.

After generating these mapping functions, we will use them to map activity cut points that were previously used in ARIC [5] from GT3X VMC measurements to Zio MAD measurements. For each participant and device, we will calculate daily amount of time in light and moderate-to-vigorous PA (LIPA and MVPA). Measures will be compared between devices using scatterplots, quantile comparisons, Pearson's correlations, and square-root mean-squared error. We will verify that our Zio cut points work well by checking that daily time spent in sedentary, light, moderate, and vigorous intensity activity are (1) highly correlated between devices and (2) have similar distributions (median and IQR) between devices.

References

[1] Davoudi, Anis, Lin Y. Chen, Jennifer Schrack, Joe Coresh, Jacek K. Urbanek. 2022. "Validation of Zio XT Patch Accelerometer for Objective Assessment of Physical Activity in Community-Dwelling Older Adults." In Progress. **Author list/order not yet finalized as work is still in progress.**

[2] Etzkorn, Lacey H., Fangyu Liu, Jacek K. Urbanek, Amir S. Heravi, Jared W. Magnani, Michael W. Plankey, Joseph B. Margolich, et al. “Patterns of Objectively Measured Physical Activity Differ between Men Living with and without HIV”. doi:10.1097/QAD.0000000000003274.

[3] Schrack, Jennifer A., Vadim Zipunnikov, Jeff Goldsmith, Jiawei Bai, Eleanor M. Simonsick, Ciprian Crainiceanu, and Luigi Ferrucci. 2014. "Assessing the "Physical Cliff": Detailed Quantification of Age-Related Differences in Daily Patterns of Physical Activity." The Journals of Gerontology. 69 (8): 973-979. doi:10.1093/gerona/glt199.

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[5] Dooley, Erin E., Lisa A. Pompeii, Priya Palta, Pablo Martinez-Amezcua, Bjoern Hornikel, Kelly R. Evenson, Jennifer A. Schrack, and Kelley Pettee Gabriel. 2022. "Daily and Hourly Patterns of Physical Activity and Sedentary Behavior of Older Adults: Atherosclerosis Risk in Communities (ARIC) Study." Preventive Medicine Reports 28: 101859. doi:10.1016/j.pmedr.2022.101859.

[6] Evenson, Kelly R., Fang Wen, Amy H. Herring, Chongzhi Di, Michael J. LaMonte, Lesley Fels Tinker, I-Min Lee, Eileen Rillamas-Sun, Andrea Z. LaCroix, and David M. Buchner. 2015. "Calibrating Physical Activity Intensity for Hip-Worn Accelerometry in Women Age 60 to 91 Years: The Women's Health Initiative OPACH Calibration Study." 2: 750. doi:10.1016/j.pmedr.2015.08.021.

[7] Choi, L., Liu, Z., Matthews, C.E., Buchowski, M.S., 2011. Validation of accelerometer wear and nonwear time classification algorithm. Med. Sci. Sports Exerc. 43 (2), 357–364. doi: 10.1249/MSS.0b013e3181ed61a3

[8] Etzkorn, Lacey H., Amir S. Heravi, Katherine C. Wu, Wendy S. Post, Jacek Urbanek, and Ciprian Crainiceanu. 2021. “Classification of free-living body posture with ECG patch accelerometers: Application to the multicenter AIDS cohort study”. bioRxiv. doi: 10.1101/2021.07.16.452654

[9] Tsai, Kao-Tai. 2022. Machine Learning for Knowledge Discovery with R. First edition ed. Boca Raton; London; New York: CRC Press. doi:10.1201/9781003205685.

[10] Karas, Marta, John Muschelli, Andrew Andrew Leroux, Jacek K. Urbanek, Amal A. Wanigatunga, Jiawei Bai, Ciprian M. Crainiceanu, and Jennifer A. Schrack. 2022. “Comparison of Accelerometry-Based Measures of Physical Activity: Retrospective Observational Data Analysis Study”. Vol. 10 JMIR Publications Inc. doi:10.2196/38077.

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? __X__ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No
(The file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No

9. **The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.** ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

___X___ Yes

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

HRV, PA, Cognition, and Dementia. (Francesca Marino, in progress.)
Ziopatch XT in PA Measurement. (Anis Davoudi, in progress. Original concept sheet submitted by Jacek Urbanek.)

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _X_ Yes ____ No

11.b. If yes, is the proposal
_X_ A. primarily the result of an ancillary study (list number __2014.18__)
___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number https://sites.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.