A. OVERALL COVER PAGE

Project Title: mHealth Center for Discovery, Optimization, and Translation of Temporally-Precise Interventions (mDOT)	
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Program Director/Principal Investigator Information: SANTOSH KUMAR , PHD **Phone Number:** 9016782487 **Email:** skumar4@memphis.edu	**Recipient Organization:** UNIVERSITY OF MEMPHIS UNIVERSITY OF MEMPHIS ADMINISTRATION 315 MEMPHIS, TN 381520001 **DUNS:** 055688857 **UEI:** F2VSMAKDH8Z7 **EIN:** 1620648618A1 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: STEPHANIE THOMPSON 315 Administration Building Memphis, TN 38152 **Phone number:** 901-678-4146 **Email:** sthmps24@memphis.edu	**Signing Official:** STEPHANIE THOMPSON 315 Administration Building Memphis, TN 38152 **Phone number:** 901-678-4146 **Email:** sthmps24@memphis.edu
Human Subjects: Yes **HS Exempt:** NA **Exemption Number:** **Phase III Clinical Trial:** NA	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will develop technologies and approaches to provide the methods, tools, and infrastructure for researchers to pursue the discovery, optimization and deployment of temporally-precise, mHealth-enabled interventions that tackle antecedent health behaviors linked to chronic diseases.

mHealth has progressed rapidly, resulting in widespread deployment of simple digital biomarkers (e.g., steps per day, sleep) to promote health and wellness. We envision a radically more powerful paradigm for applying mHealth to maintain health and managing the growing burden of chronic diseases, specifically, temporally-precise interventions that are individualized to the moment-to-moment context of each individual to directly manage, treat, and prevent medical conditions. The rapidly growing array of mHealth biomarkers captures the temporal dynamics of an individual’s state, behaviors, and surrounding environment that drive cumulative risk for an individual’s total disease burden. But, we lack the tools to discover which (combinations) of these continuous biomarkers are the most relevant, at different moments, for selecting the target risk driver(s) and deciding the delivery timing of sensor-guided interventions. Current mHealth interventions derive largely from expert knowledge and are usually not optimized for long-term engagement in self-care. Further, they either lack personalization, or if personalized, learn slowly. Finally, personally optimized, temporally-precise mHealth interventions will improve health outcomes only if they can be deployed at scale. Real-life deployment of increasingly complex mHealth interventions that can leverage a growing number of biomarkers to optimize the selection, adaptation, and timing of intervention delivery, is challenged by limited battery and compute capacity, the emergence of high data rate sensors, and the need to ensure privacy and data security. The mDOT Center will realize its vision through the following specific aims:

Aim 1: Enable the discovery, optimization, and translation of temporally-precise mHealth interventions via three technology research and development cores (TR&D).

Aim 2: Collaborate with investigators of a diverse array of collaborative projects (CP) and service projects (SP) to engage the health research community in joint development, iterative evaluation, and broadening impact.

Aim 3: Maximize the scientific and societal impact via technology training and dissemination (TT&D).

Aim 4: Provide the managerial and operational structures for mDOT to achieve its research, development, collaboration, training, and dissemination goals.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The mDOT Center disseminates information to communities of interest via its website, mdotcenter.org, which is updated on a regular basis and also when events warrant (more than 13,000 pageviews since launch on July 1, 2020).

Recordings of webinars are posted to the mDOT Center's YouTube channel, where they are accessible by the general public; more than 22 hours of training videos have been released. More than 220 videos posted on the mDOT Center's YouTube channel have been viewed a total of more than 44,600 times on the channel, which now has more than 300 subscribers and more than 3,800 hours of watch time.

A second website, mhti.md2k.org, exists for the purpose of providing information about the upcoming NIH mHealth Summer Training Institute and has received 12,700 users and over 41,100 page views through September 2022.

A third website, mHealthHUB, serves as a portal for the greater mHealth community (more than 48,600 unique users and nearly 163,000 pageviews since its November 2015 launch).

mDOT Center investigators have published or have submitted and under review 39 papers related to mDOT Center research. A full list of these publications by mDOT Center investigators can be found in section B.2.

In addition, mDOT Center investigators have participated in 103 talks and presentations at 110 global meetings.

mDOTCenter.org: https://mdotcenter.org/

mHealth Training Institute: https://mhti.md2k.org/

mHealthHub: https://mhealth.md2k.org/

mDOT Center GitHub Repository: https://github.com/MD2Korg/

mDOT Center YouTube Channel: https://www.youtube.com/c/mdotcenter

mDOT Center LinkedIn: https://www.linkedin.com/in/mdotcenter/

mDOT Center Reddit: https://www.reddit.com/user/mDOT_Center/

mDOT Center TikTok: https://www.tiktok.com/@mdotcenter

Presentations & Workshops:
S. Kumar, "Challenges and Opportunities in Trustworthy AI for Health and Wellness" ACM SIGKDD Trustworthy AI Day, 08/15/22.
S. Kumar, "Detecting and Characterizing Stress in Daily Life," Keynote Speech at IEEE EMBC Workshop on Detection of Stress and Mental Health Using Wearable Sensors, 07/11/2022.
S. Kumar, "Can Sharing Anonymous Wrist-worn Accelerometry Data Re-identify You," EECS Department, University of California, Irvine, 06/03/2022.
S. Kumar, "Can Sharing Anonymous Wrist-worn Accelerometry Data Re-identify You," CSE Department, The Ohio State University, 04/29/2022.
S. Kumar, "Persuasive AI to Improve Health and Wellness," Indo-US Roundtable, 03/24/2022.
S. Kumar, "Wearable AI for Designing, Optimizing, and Delivering Temporally-Precise mHealth Interventions," mHealth Special

Session at International Conference on Network, Systems, and Security (NSySs'21), 12/23/2021.
S.N. Shukla. Heteroscedastic Temporal Variational Autoencoder For Irregularly Sampled Time Series. International Conference on Learning Representations. 4/27/2022.
Harnessing real world behavior data to optimize treatment delivery. ABCT 56th Annual Convention, New York, NY November 20, 2022
Acceptance Lecture, 2021 Van Wijngaarden Award, Centrum Wiskunde & Informatica, Amsterdam, Netherlands, November 3, 2022 (ceremony postponed from last year due to COVID)
Inference for Longitudinal Data After Adaptive Sampling. 2022 Al-Kindi Distinguished Statistics Lecture, King Abdullah University of Science and Technology, Saudi Arabia, October 20, 2022
We used Reinforcement Learning; but did it work? 2022 Al-Kindi Distinguished Statistics Lecture, King Abdullah University of Science and Technology, Saudi Arabia, October 19, 2022
Data, Personalization, Digital Health! Quantitative Science Grand Rounds, Moffitt Cancer Center, Tampa, FL. October 5, 2022
Inference for Longitudinal Data After Adaptive Sampling. Wellner Lecture, University of Idaho, Moscow, ID September 29, 2022
Panelist, launch event for the Kempner Institute for the Study of Artificial and Natural Intelligence, Harvard University, September 22, 2022
Inference for Longitudinal Data After Adaptive Sampling. Operations Research & Financial Engineering Department Colloquium, Princeton University, Princeton NJ, September 13, 2022
We used RL; but did it work? S.S. Wilks Memorial Lecture, Princeton University, Princeton NJ, September 12, 2022
We used RL; but did it work? Workshop on Reinforcement Learning at Harvard, Center for Brain Science, Harvard University, August 30, 2022
Data, Personalization, Digital Health! Keynote. European Health Psychology Society Conference, Bratislava, Slovakia, August 26, 2022
Inference for longitudinal data after adaptive sampling, Keynote, ICSA 2022 Applied Statistics Symposium, Gainesville, FL, June 22, 2022
Data, Personalization, Digital Health! Keynote (virtual). Society for Ambulatory Assessment Conference, June 14, 2022
Inference for Longitudinal Data After Adaptive Sampling. Keynote, 35th New England Statistics Symposium (NESS), University of Connecticut, Storrs, CT, May 24, 2022
Assessing Personalization in Digital Health. Charles L. Odoroff Memorial Lecture, University of Rochester Medical Center, Rochester, NY, May 19, 2022
Optimizing Your Digital Health JITAI using a Micro-Randomized Trial, ECNP Digital Health Network, online, Get Digital Talk, May 10, 2022
Assessing Personalization in Digital Health. Invited virtual talk, Deutsche ArbeitsGemeinschaft Statistik (DAGStat 2022), Hamburg, Germany, March 29, 2022
We used Reinforcement Learning, but did it work? Virtual keynote, AI for Behavior Change workshop, AAAI 2022, February 28, 2022
We used Reinforcement Learning; But Did It Work?, AI Talk (virtual), Chalmers University of Technology, Gothenburg, Sweden, January 19, 2022
We used Reinforcement Learning; but did it work? Virtual presentation, CIS Colloquium, EPFL, December 13, 2021
Counterfactual inference in sequential experimental design. Poster. Royal Statistical Society International Conference (2022), Aberdeen, Scotland, September 13, 2022
Generalized Kernel Thinning, JSM 2022, Washington DC, August 10, 2022
Greedy Approximation Algorithms for Active Sequential Hypothesis Testing. Simons Institute Workshop Quantifying Uncertainty: Stochastic, Adversarial, and Beyond, Berkeley CA, September 12, 2022.
Statistical Inference After Adaptive Sampling for Longitudinal Data. INFORMS 2022, Indianapolis, IN, October 17
Designing Reinforcement Learning Algorithms for Digital Interventions: Pre-implementation Guidelines. International Chinese Statistics Association Applied Stats Symposium. Talk in the session Precision Digital Health Care via Machine Learning, Gainesville, FL, June 21, 2022
An Algorithm to Determine Treatment Timing in Mobile Health: Design and Evaluation. INFORMS 2022, Indianapolis, IN, October 2022
Assessing the Effectiveness of a Sampling Algorithm for Just-in-Time Intervention Delivery. Virtual talk in the contributed session Adaptive Design/Adaptive Randomization, ENAR 2022, March 28, 2022

RL Digital Interventions Under User Heterogeneity: A Bayesian Nonparametric Approach. Poster, RLDM 2022, Providence, RI, June 9, 2022.
Near-optimal compression in near-linear time. Poster. Royal Statistical Society International Conference (2022), Aberdeen, Scotland, September 13, 2022
Generalized Kernel Thinning, JSM 2022, Washington DC, August 10, 2022
Revisiting minimum description length complexity in overparameterized models. Symposium on Algorithmic Information Theory & Machine Learning, Alan Turing Institute, London, UK, July 4.
Near-optimal compression in near-linear time. Talk at the Kernel Methods for Numerical Integration mini-symposium, 2022 SIAM Conference on Uncertainty Quantification, April 14, 2022
Imputation with nearest neighbors for adaptively collected data, Foundations of Data Science Institute Retreat 2022 (virtual), January 6
Distribution compression in near-linear time. Contributed poster. 4th Symposium on Advances in Approximate Bayesian Inference, February 2

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

TR&D1
Towards fulfilling Specific Aim 1, we will leverage our progress in developing novel imputation methods and mount an attack on the problem of inference in hierarchical biomarker computation graphs. This will tackle the fundamental problem of deciding where to perform impute, given a complex biomarker computation in which some of the inputs exhibit missingness. As part of this work we will develop a unified imputation approach for irregularly-sampled data. Towards fulfilling Specific Aim 2, we plan to continue working on developing the mRisk method with CP1 and CP5 to improve the mRisk model so that it is able to use the self-reported smoking lapses that are not supported by puffMarker detection and hence are missing the precise timing of lapse. Second, we plan to apply the mRisk model to all datasets generated in CP1 and CP5 so our health research collaborators can use it to analyze risk characteristics and pursue their publications. Third, we plan to implement the real-time version of mRisk towards the design and development of new mHealth interventions.

TR&D2
In Year 3 CP2 and CP8 will run clinical trials deploying our RL algorithms. These RL algorithms will pool data (Aim 2) across individuals in order to personalize. We will finalize and provide a protocol for the algorithms. Further both algorithms will be using approaches developed under Aim 1 to allow the RL algorithm to account for delayed effects. These trials will allow for the first real-life evaluations of the RL algorithmic research conducted under Aims 1,2. We will continue the work (in collaboration with CP3) of the toolbox. CP3 will conduct a user study that will then allow us to refine the toolbox. This toolbox will allow us to more effectively disseminate our RL algorithm developments. We aim to have a first version for use by health scientists and in particular our SPs this year. We aim to start making greater progress on Aim 3, particularly with regard to the use of intermediate outcomes of treatments by the RL algorithm. This work will also involve generalizing RL algorithms to be able to accommodate both delayed observations of state and reward. We will continue to work on integrating research themes from TR&D1 into TR&D2 via studying the effects of uncertainty on RL methods for problems with delayed treatment effects.

TR&D3
We will continue the two activities that we initiated this year and which are still on-going: understanding re identification risks from sharing processed sensor data, and understanding factors that affect users' perception of privacy with wearable and ambient sensor devices monitoring biomarkers and delivering interventions. We will build upon our work on platform-aware neural architecture search to consider architecture search for neuro-symbolic models (that combine neural models with first-principles/physics) on ultra-resource constrained platforms. Going beyond privacy-aware sharing of data for biomarker computation, we will examine privacy and trust issues in the full sensing-biomarker-intervention-delivery loop across edge-cloud. Specifically, we will target (i) Risks from predictions different from past/present, which can't be defended with counter-evidence, difficult to explain; (ii) Ensuring delivery of intervention to valid user, which requires continually authenticating the user; (iii) Delivering intervention in a privacy-sensitive manner, which would require adapting delivery to device (wearable, mobile, ambient) and modality (visual, acoustic, haptic) and context (e.g., presence of others, location, physical state, etc.); and (iv) Challenges arising from interventions that use explore-exploit paradigm (e.g., deep reinforcement learning) that depends on "probes", such as leak of information about personal preferences, behaviors, and contexts.

TT&D

We will write up and publish the analysis of the 2022 mHTI to advance Team Science. We will organize and conduct the 2022 mHTI. We will reorganize the mHealthHUB portal and website. We will continue with mDOT Center-branded online webinars. We will deploy the CTSI/Vanderbilt-developed Flight Tracker software to automate tracking and analysis of career outcomes, including transdisciplinary collaborations, publications, funding, training activities, and other milestones of the mHTI scholars. We will utilize the longitudinal data to analyze the short-term and long-term causal effects of the mHTI on the mHTI scholars' academic collaboration for journal papers and grant writing with other mHTI and/or non-mHTI scholars. We plan on two types of causal evaluations: (1) evaluate the value-added of the mHTI by assessing within-person changes over time using the difference-in-difference design; (2) evaluate the impact of the mHTI program using a quasi-experimental design by comparing mHTI scholars and non-scholars with similar background characteristics regarding their collaboration activities.

Software

The pJITAI platform is slated to be completed during this next year and be tested as part of an mHealth-based behavioral study. Currently, a user-study with behavioral scientists is underway to test the user interfaces that have been designed. Once this study is complete and the interfaces finalized, these will be incorporated into the pJITAI web interface. We are currently iterating on the Thompson Sampling algorithm's implementation to ensure that it is implemented in the most efficient and straightforward method since we would like this to become a template for others to utilize when building new algorithms. We anticipate having a fully functional system by the end of 2022 when we can hand off the platform to our CP partner for pilot testing and ultimately a full field study deployment. The mDOT team will continue to refine and adjust the software based on our experience with this real-world trial. By the end of this year's reporting period, we would like to have this software near completion and make it available to anyone wishing to utilize the technology or to enhance it with their own algorithms.

We will build the mRisk modules to expand the capabilities and potential utility of mDOT-MIND framework for smoking cessation intervention research. In addition to detecting stress in real-time, the smartwatch app will include new AI-based models to detect smoking events. The smartwatch model will include a new capability to estimate the risk of a smoking lapse continuously in newly abstinent smokers. We are currently working on building these models based on other MD2K-based data sets before transitioning them into a format suitable for deployment on a smartwatch-based platform. The smartwatch platform will be complemented with additional modules on the smartphone when data aggregations are necessary. During this year, we plan to recruit new collaborative projects based on this platform in order to refine and test the implementation under real-world conditions.

The team is also working on a new mHealth risk assessment tool to help researchers understand the risks and challenges associated with utilizing mobile sensors (e.g. accelerometer, gyroscope, PPG) in human subjects research. This tool will aid those researchers by providing them feedback and information regarding the risks to their subjects based on those risks that have been published by the greater research community.

ADMIN

The Admin Core will continue to provide administrative, managerial, and infrastructure support to enable the mDOT Center to accomplish its Year 3 goals in research, training, and dissemination activities, in addition to continuing its successful strategies for communication and management.

B.2 What was accomplished under these goals?

B.2.1. - TR&D1 - DISCOVERY

In Year 2, the TR&D1 undertook a variety of activities (as described below) to fulfill its goals. We extended our previous deep learning approach, Multi-Time Attention Networks, to enable improved representation of output uncertainty. Our new approach preserves the idea of learned temporal similarity functions and adds heteroskedastic output uncertainty. We have also been developing a toolbox for the specification and estimation of mechanistic models in the dynamic bayesian network family, BayesLDM. This toolbox focuses on making it easier to specify probabilistic dynamical models for time series data and to perform Bayesian inference and imputation in the specified model given incomplete data as input. TR&D1 also completed an investigation of a deep learning-based approach to the imputation of pulsative biophysiological signals such as ECG and PPG, which are defined by a quasiperiodic morphology in terms of "beats'' that are derived from the cyclic action of the cardiovascular and cardiopulmonary systems. The novel PulseImpute dataset is the first large-scale dataset containing complex imputation tasks for pulsative biophysical signals. TR&D1 also completed the development of a novel continuous-time attention model which is capable of learning multimodal densities, meaning that the attention density can be focused on multiple signal regions simultaneously. We completed the development of a novel continuous-time attention model which is capable of learning multimodal densities, meaning that the attention density can be focused on multiple signal regions simultaneously. TR&D1 developed a new model to estimate composite risk smoking lapse in newly abstinent smokers. A fully developed first version of this model, called mRisk, was evaluated on a dataset of 92 participants who were newly abstinent smokers. Finally, TR&D1 developed a transformer-based deep learning architecture for predicting nonresponse given a history of past EMA responses in conjunction with demographic and contextual data. We worked to explore the utility of transformers on EMA data in general and for non-response prediction as opposed to traditional machine learning methods. In Year 2, TR&D1 worked with CP1, CP3, CP4, CP5, CP8, and SP2.

B.2.2. - TR&D2 – OPTIMIZATION

In Year 2, the TR&D2 undertook a variety of activities (as described below) to fulfill its goals. Our most significant breakthrough was the successful development of the mathematical theory that provides measures of confidence when the Reinforcement Learning (RL) algorithm pools data across individuals in order to personalize during a clinical trial. We are now able to further develop and deploy this type of algorithm in clinical trials. This is a major step forward for the use of personalization algorithms in mHealth clinical trials. TR&D2 also was responsible for the development of an RL algorithm and inference from a Micro-Randomized Trial (MRT) employing an RL algorithm, spurred on by our collaborations with CP2 and CP8. We are developing and will deploy an RL algorithm that autonomously pools data across individuals in order to personalize the mHealth intervention to each individual during the study. Also, TR&D2 is designing an mDOT Center toolbox called pJITAI that health scientists can use to design their RL algorithm for use in conducting their mHealth study in collaboration with CP3. Finally, TR&D2 is working to generalize current myopic Bandit RL methods to enable learning non-myopic decision rules that account for delayed intervention effects by working with TR&D1 and CP3 to investigate the application of deep learning-based RL methods to RL simulation environments based on key properties of contextualized messaging interventions. In Year 2, TR&D2 worked with CP 1, CP2, CP3, and CP8.

B.2.3. - TR&D3 - TRANSLATION

In Year 2, the TR&D3 undertook a variety of activities (as described below) to fulfill its goals. TR&D3 continued our work in learning autoencoder structures to extract heart rate and heart rate variability information from multichannel sensor data, while stripping information that is sensor- or subject-related information not relevant to the inference tasks at hand. We also explored RF imaging to create signal processing architectures to support biomarker computations on resource-constrained high data rate sensor arrays. Our findings on prototype implementation of the mircomarker framework on the MotionSense HRV platform show that PPG data can be compressed into micromarkers with low latency while retaining virtually identical performance (as compared to uncompressed data) in tachogram signal estimation. TR&D3 also refined its creation of the next generation of the MotionSense HRV unit having developed a dual-core version of our wristband and rewrote the software stack from the ground up to support common machine learning abstractions often encountered in bio/micro marker implementations. We performed detailed analysis on techniques for optimizing the model and memory utilization of the deployed model in the system. The firmware was further modified to be backward compatible with previous versions and our prototype implementation shows that micromarker framework and classical feature extraction methods can coexist on the MotionSense HRV device by allowing multimodal sensor data to be transformed into biomarkers of interest. Also in this project period, we developed a multiple transmit-receive radar system using 2 phase-locked loop systems to generate frequency sweeps in the frequency band of 500 MHz to 6 GHz that is suited for interrogating biological tissues. This radar system will be applied to imaging and sensing the cardiac muscle movement to assess the contractility strength by utilizing multiple array elements covering the thoracic cavity and allows for implementation of scalable 2D BioRF sensor arrays that can be tailored to different applications. TR&D3 also developed and released THIN-Bayes, an open-source software tool for neural architecture search for wearable devices employing resource-constrained microcontrollers. THIN-Bayes makes use of hardware-in-loop with bayesian optimization and demonstrates levels of performance that far outperforms the state of the art. Another focus during Year 2 was on understanding and quantifying privacy risks from sharing processed wearable sensor data with local low-power computing resources that would allow mapping a sequence of raw sensor measurement sequence to a sequence of higher semantic value data products such as inferences, micromarkers, engineered features, and embeddings. Preliminary findings from the research on quantifying reidentification risks from sharing processed motion sensor data suggest that modern machine learning methods allow reidentification to be done successfully when temporal characteristics are retained. Finally, TR&D3 conducted an online study of 122 participants from the USA to find what factors affect the privacy perception of a user regarding a device or a sensor. Our findings show that a user's perception of privacy not only depends upon the data collected by the sensor but also on the inferences that can be made on that data, familiarity with the device, its form factor, as well as the control a user has over the device design and its data policies. In Year 2, TR&D3 worked with CP1, CP3, CP6, and CP7.

B.2.4. – SOFTWARE

In Year 2, we developed an overarching vision for the software to be developed by the mDOT Center - the mDOT-MIND (mHealth Intervention Delivery) software platform. The MIND platform is a suite of software products that all contribute, in part, to the delivery of optimized mHealth interventions to participants in a field environment. We collaborated with CP7 to deploy it in a fully remote user study on identifying the sources of stress that can be automatically detected by wearable devices such as a commercially available smartwatch. The study was called the MOODS (Mobile Open Observation of Daily Stressors) study. The modules in the first version of the MIND software include a set of components that implement an IRB-compliant informed consent process for smartphones which can be reused in subsequent and additional studies with minimal changes. Additionally, wearable AI technology that measures and prompts based on participant's individual stress and non-stress episodes was built for Fossil smartwatches running WearOS. The real-time stress detection on the Fossil smartwatch was used to generate prompts in real-time based on parameters that were initially based on population data, but were gradually personalized to be optimal for each participant, to simulate an MRT trial. The second major software in the mDOT-MIND platform is a standalone system designed for both software engineers and behavioral scientists as a way to include reinforcement learning into their mHealth field studies. The MOODS study software has now been successfully used by 140 participants. Finally, the mDOT Software Team began the design and development of a new modular cloud-based technology stack to support reinforcement learning by working with TR&D2. This tool is a way for behavioral scientists and engineers to collaborate on designing and implementing personalized just-in-time interventions (pJITAIs), composed of three distinct components which have been prototyped and iterated on during this project period. Once completed, this tool is expected to be deployed by the researchers in CP3 as part of a pilot study without any direct involvement by mDOT Center software staff.

B.2.5. - TRAINING & DISSEMINATION

Due to the ongoing COVID pandemic, the training activities were again primarily conducted virtually. The main focus of the training was the development and conduct of a virtual version of the annual mHealth Training Institute (mHTI). This entailed deployment of a virtual events platform (Zoom) and a comprehensive, online application management system (SmarterSelect). The training activities were augmented by the participation of the CERES (Connecting the EdTech Research Ecosystem) collaborative: a UC-Irvine based Center dedicated to training and developing research ways to reduce widening disparities in learning and development due to unequal access and personalization of digital technology across populations and contexts (https://ceres.uci.edu/). From a pool of 232 applicants, 30 were chosen as scholars for the 2022 mHTI. A corresponding group of faculty, comprising both academics and NIH Program Officers was also recruited. The virtual 2022 mHTI was conducted between May 2 and July 28, 2022 and comprised a series of core lectures, seminars as well as mentored team activities. In addition to the mHTI-related lectures, the TT&D core conducted a series of webinars on themes of interest to the broader mDOT Center community. To increase the national and international impact of the mDOT Center, the webinar series has recruited faculty from institutions abroad including the UK, Switzerland, and New Zealand.

B.2.6. - ADMINISTRATION CORE

The mDOT Center Operations Office, housed in Memphis, Tenn., is the main hub for mDOT Center administration. The Center is structured to include full-time operations management, business management, administration, and communications staff, who are collectively responsible for the day-to-day management of the Center, including providing support for the activities of the investigators. In Year 2, as recommended by our Executive Advisory Committee, the admin team launched a multifaceted digital media campaign to ensure that the mDOT Center had a unique brand and online presence with clear imaging and messaging to construct a similar, or better, brand recognition as the previously successful MD2K Center. A few of these items included the creation of new accounts on three popular social media platforms: LinkedIn, Reddit, and TikTok to make training content more accessible and to broaden the audience to include the general public, while existing Twitter and YouTube profiles were updated with logos, graphics, and wording to emphasize the mDOT Center. In addition, mDOT Center content was promoted on our various social media platforms with short blurbs to make it more attractive and digestible to our audience. The mDOT Center Admin Team was also tasked with facilitating brainstorming sessions across the TR&Ds. The Center held dedicated TR&D Synergy Conference Calls in the month of April 2022. The Admin Core also hosted an in-person TR&D1 team meeting in Memphis in May 2022. The Admin Core will also host the all-hands Annual Center Meeting in-person in November 2022. The mDOT Center added a new Collaborative Project in Year 2 expanded that will enhance the research being doing done in TR&D1 and TR&2: CP8 - The Center for Methodologies for Adapting & Personalizing Prevention, Treatment and Recovery Services for SUD & HIV (MAPS Center), led by Dr. Inbal Nahum-Shani at the University of Michigan and funded by NIDA until 2026. The mDOT Center also added a new Executive Advisory Committee member in Year 2. We recruited Dr. David Mohr, Professor, Preventive Medicine (Behavioral Medicine), Medicinal Social Sciences, & Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine to advise the Center's TR&D2 team that develops personalized interventions and wanted to work more closely with behavioral health researchers. Dr. Mohr now helps to provide a voice from that community to better assess the value and utility of products coming from TR&D2 for health research. Finally, The mDOT Center admin team facilitated hosting the all-virtual mHealth Training Institute (mHTI) where mHealth training was offered to 35 scholars with 29 faculty from 20 institutions in 11 disciplines, conducted in an all-virtual environment over 13 weeks. The mDOT Center Admin Core was responsible for the hosting, setup, entire backend and technical components of the all-virtual 2022 mHTI.

B.3. Center Highlights

B.3.1. Dealing with Missing Data in mHealth: mHealth interventions are expected to work robustly in the daily life, where sensor data may suffer from poort quality, large missingness, and uncertainty in inferences of human states and their contexts due to imperfect machine learning models. Similarly, self-report data may also be subject to biases and non-responses. In Year 2, the mDOT Center developed several novel methods, tools, and datasets to improve the handling of missing data. First, Heteroskedastic Variational Autoencoders (HetVAE) was developed to improve the representation of output uncertainty that preserves the idea of learned temporal similarity functions and adds heteroskedastic output uncertainty. Its codebase was released publicly. Second, we developed a new toolbox called BayesLDM to make it easier to specify probabilistic dynamical models for time series data and to perform Bayesian inference and imputation in the specified model given incomplete data as input. The toolbox and user guides were released publicly. Third, we developed state-of-the-art attention-based deep learning transformer architecture called PulseImpute that can learn to leverage the quasi-periodic signal structure inherent to many biophysiological signals to perform accurate imputation in the face of substantial amounts of missingness. We curated the largest clean ECG and PPG datasets that will be released publicly in Year 2. Imputations can reliably be done on only relatively small segments of missing data and hence can't make the entire time series data collected from the daily life free of gaps. As the fourth innovation, to better model missingness in time series data, we introduced kernel deformed exponential families as more flexible attention mechanism that can more often capture the most salient aspects of an input signal by focusing on multiple signal regions simultaneously.

S.N. Shukla, B.M. Marlin. Heteroscedastic Temporal Variational Autoencoder For Irregularly Sampled Time Series. In Proceedings of the International Conference on Learning Representations. 2022.

Tung, K., Torre, S.D., Mistiri, M.E., Braganca, R.B., Hekler, E.B., Pavel, M., Rivera, D.E., Klasnja, P., Spruijt-Metz, D., & Marlin, B.M. (2022). BayesLDM: A Domain-Specific Language for Probabilistic Modeling of Longitudinal Data. Accepted at IEEE/ACM international conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE) 2022. ArXiv, abs/2209.05581.

M. A. Xu, A. Moreno, S. Nagesh, V. B. Aydemir, D. W. Wetter, S. Kumar, and J. M. Rehg. PulseImpute: A Novel Benchmark Task for Pulsative Physiological Signal Imputation. Proceedings 36th Conference on Neural Information Processing Systems (NeurIPS), Track on Datasets and Benchmarks, 2022. Accepted for publication. NIHMS1839168.

B.3.2. Optimal Personalization of mHealth Interventions via Reinforcement Learning (RL): Each individual is unique in their physiology, behavior, context, and preferences. For an intervention to have a better chance to work for each individual, it needs to be personalized. But, unlike e-commerce where there is a large volume of users and digital traces, in mHealth the trials are small in size, they are conducted for a limited time, and hence the amount of data available for personalization is very small in magnitude. In Year 2, we made a major advancement in developing methods for achieving personalization despite the above limitations. The basic idea is to autonomously pool data across individuals in order to personalize the mHealth intervention to each individual during the study. This pooling of data by the RL algorithm produces dependence between individuals in the studies (called "adaptive sampling"). This is highly problematic as these are/will be registered clinical trials and thus primary data analysis methods must be justified and pre-specified. It was incumbent on our team to develop the mathematical theory and associated statistical methodology/measures of confidence that allow our collaborators to pre-specify the primary data analysis methods before they conduct these clinical trials. The mathematical theory is non-trivial. We are thrilled to report that we have successfully developed the theory! Autonomously pooling of data to learn faster can now be used in real-life trials.

A. Trella, K. Zhang, I. Nahum-Shani, V. Shetty, F. Doshi-Velez, S. Murphy. Designing Reinforcement Learning Algorithms for Digital Interventions: Pre-implementation Guidelines. Algorithms 2022, 15(8), 255.

A. Trella, K. Zhang, I. Nahum-Shani, V. Shetty, F. Doshi-Velez, and S. Murphy. Reward Design For An Online Reinforcement Learning Algorithm Supporting Oral Self-Care.

K. Zhang, L. Janson, S. Murphy. Statistical Inference After Adaptive Sampling in Non-Markovian Environments.

B.3.3. mHealth Intervention Delivery (MIND) Software Platform: The MIND platform is a suite of software products that all contribute, in part, to the delivery of optimized mHealth interventions to participants in a field environment. The suite consists of (1) an app for commercial smartwatches that implement AI models for detecting health of behavioral state in real-time, (2) a cross-platform app for smartphones that anyone can install on their personal phones (both Android and iOS) which can generate real-time triggers for self-report or intervention based on the detection of events, risks, or changes in states on the smartwatch and/or the smartphone, and (3) a cloud system that can communicate with both the smartwatch and smartphone app to receive data uploads and send decisions or updated criteria for generating prompts. This software was used to successfully conduct a fully remote user study on identifying the sources of stress that can be automatically detected by wearable devices such as a commercially available smartwatch. The software was piloted, revised, tested, and successfully used by 140 participants for up to 100 days to monitor stress and report the sources of stress for events detected by the MIND smartwatch app in real-time. We are now exploring extending this software for use in potential new CP's and SP's that are interested in stress, stressors, and stress-triggered interventions. We also plan to expand this software suite to continuously monitor risk for smoking lapses by wearables and conduct micro-randomized trials (MRT's) to find best new interventions for smoking cessation.

B.3.4. CENTER SUMMARY TABLE   Grant Number: P41EB028242   Reporting Period: (12/01/2021 - 11/30/22)

	TR&D Projects	Collaborative Projects	Service Projects	Training & Dissemination	TOTAL
Number of Publications*	14	8	4	2	24*
Number of Patents	0	0	0	0	0
Number of Investigators	36	9	8	26	79
% of Center Funds Allocated	78%	8%	3%	11%	100%
% of Center Funds for AIDS	0%	0%	0%	0%	0%
Service Fees Collected ($)					

Some publications overlap between CPs & SPs, as they were published in collaboration with multiple projects

The mDOT Center assembled a high-profile External Advisory Committee (EAC) that includes 5 thought leaders, each representing an expertise in different domains of research and operations.

Dr. David Kennedy, Professor of Psychiatry at UMass Medical School – Dr. Kennedy is an expert in neuro-informatics, known for his contributions to the advent of MRI-based morphometric analysis, functional MRI, and diffusion tensor pathway analysis. He is the PI of P41 Center called the "Center for Reproducible Neuroimaging Computation (CRNC)". He is advising the mDOT Center on its administrative and training activities.

Dr. Jimeng Sun, Professor of Computer Science at the University of Illinois at Urbana Champaign (UIUC) – Dr. Sun develops AI for Healthcare who is known for contributions in deep learning for drug discovery, computation phenotyping, clinical predictive modeling, treatment recommendation, and clinical trial optimization. He is advising the mDOT Center's TR&D1 team on uncertainty-aware modeling of personalized risk dynamics from sensor-derived biomarkers to enable the discovery of new mHealth interventions.

Dr. Veena Misra, Distinguished Professor of Electrical and Computer Engineering at North Carolina State University (NCSU) – Dr. Misra is an expert in ultra-low power and self-powered biosensor design, hybrid silicon-molecular electronics, and nano-magnetics. She is the PI of NSF Nanosystems Engineering Research Center (ERC) on Advanced Self-Powered Systems of Integrated Sensors and Technologies (ASSIST). She is advising the mDOT Center's TR&D3 team on sensor and signal processing architectures to support resource-efficient real-time computation of complex biomarkers on resource-constrained high data-rate sensor arrays.

Dr. Jason Hong, Professor in the HCI Institute in School of Computer Science at Carnegie Mellon University (CMU) – Dr. Hong works at the intersection of human-computer interaction (HCI), privacy, security, and computing systems. His work discovers novel utility of sensors for improving human lives while making security and privacy easier for every human. He is advising the mDOT Center team on ensuring users' behavioral privacy and anonymity during mHealth biomarker data analytics, optimization of sensor-triggered mHealth interventions, and real-life deployment of mHealth interventions.

Dr. David Mohr, Professor, Preventive Medicine (Behavioral Medicine), Medicinal Social Sciences, & Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine – New to the EAC this year, Dr. Mohr's work lies at the intersection of behavioral science, technology, and clinical research, focusing on the design and implementation of interventions that harness digital technologies to promote mental health and wellness. He is well versed in the use of data from smartphone and wearable sensors to identify behavioral and psychological targets that can be used for intervention. Dr. Mohr is advising the mDOT Center's TR&D2 team that develops personalized interventions and wants to work closely with behavioral health researchers. Dr. Mohr now helps to provide a voice from that community to better assess the value and utility of products coming from TR&D2 for health research.

Recruitment was deliberate to balance demographics to further ensure a diversity of perspectives and experiences among committee members. The EAC provided the high-level guidance, oversight and review of progress towards research and training goals and the efficacy of Center operating structures and policies for Year 2. This group also provided future-oriented feedback on mDOT Center research and training directions as well as helping to establish new connections for the center that can extend the impact and reach of our activities.

The EAC meetings took place virtually using the Zoom teleconferencing system. Each Committee Member was individually presented an overall view of the mDOT Center and other aspects of research that were tailored to their interests and expertise (schedule below). The EAC's next meeting will be convened as a group with all 5 members at the mDOT Center's Annual Meeting. The EAC has provided the below report to team members regarding the planned implementation of specific guidance received or alternate strategies to be pursued as the mDOT Center heads into Year 3.

- Dr. Jimeng Sun reviewed the mDOT TR&D1 on 8/24/2022
- Dr. David Kennedy reviewed the mDOT Training and Administrative Core on 8/25/2022
- Dr. Veena Misra reviewed the mDOT TR&D3 on 8/31/2022
- Dr. Jason Hong reviewed the mDOT Privacy Components on 8/31/2022
- Dr. David Mohr reviewed the mDOT TR&D2 on 9/1/2022

mDOT Center Review
from Dr. Jimeng Sun
Project Period 2 (12/01/2021 – 11/30/2022)

1. OVERALL CENTER STRUCTURE & DIRECTION

Notable Strengths
SUN:

- ***Strong leadership and center organization in tackling challenging research tasks in mHealth***
- ***Well-organized research activities***
- ***Highly coordinated research plan that involve multiple institutions but still work as a coherent team***

mDOT RESPONSE: Thank you for your kind words.

2. TR&D1-DISCOVERY STRUCTURE & DIRECTION

Notable Strengths
SUN:

- ***Extremely high-caliber researchers that are well-known in their respective domain***
- ***All groups have demonstrated solid research output over the year***
- ***The teams have systematically addressed all my comments from last review. This confirmed the project team and leadership are extremely well-organized and attend to details***

mDOT RESPONSE: Thank you for your kind words.

Other Comments
SUN:

- ***Multiple projects in the centers are producing valuable datasets that could be impactful if they can be shared and publicized to the broader research community. This might be a wild idea and***

completely optional but if resource is available, it could be beneficial to organize some data challenges using the datasets produced in different projects.

mDOT RESPONSE: This is a very good suggestion. We indeed have been thinking about this. We have previously released wrist-worn motion sensor data collected for seven days in the field environment with time-synchronized annotation of brushing and flossing activities. We are now collecting a new dataset on momentary stress events detected by wearables and the sources of such momentary stress. The data from this study is also consented to be made public. We would love to think how to organize some challenges from these datasets.

3. CP RESEARCH: STUDENT WORK (PULSEIMPUTE) - GEORGIA TECH

Notable Strengths

SUN:

- ***Continuous monitoring data are important for mHealth applications***
- ***Realistic imputation of continuous waveforms are challenging tasks***
- ***The bottleneck dilated convolution model seems appropriate for this task***

mDOT RESPONSE: Thanks for this positive feedback.

Other Comments

SUN:

- ***It will be good to design more quantitative metrics to evaluate the quality of the imputed signals***

mDOT RESPONSE: This is a good suggestion, we will investigate additional metrics with a particular focus on quantifying the quality of the reconstructed signal morphology, which can complement the standard L2 measure.

4. CP RESEARCH: STUDENT WORK (MODELING WITH BAYESLDM) - UMASS

Notable Strengths

SUN:

- ***Missing data is a common and tricky problem in mHealth***
- ***Solid theoretical foundation with Bayesian mechanistic models***

mDOT RESPONSE: Thanks for this feedback on the project.

Other Comments

SUN:

- ***It will be great to share the dataset or the data simulator to the public.***

- **mDOT RESPONSE:** The real data sets used to demonstrate the BayesLDM system use data from the ongoing HeartSteps II trial (CP3). CP3 does plan to make data available to the research community when the study concludes. The BayesLDM Github repository does include a range of example models using synthetic data and includes the data generating simulators.

5. CP RESEARCH: STUDENT WORK (mRISK) - MEMPHIS

Notable Strengths

SUN:

- ***Smoking lapse is an important problem for mHealth***
- ***Leveraging multi-modality data is novel and necessary for this research***
- ***Impressive amount of real-world data is being collected***
- ***The proposed deep learning model seems effective in their evaluation***

mDOT RESPONSE: Thank you for your kind words.

Other Comments
SUN:

- ***It will be good to study how to handle the missing and erroneous data as they are common in mHealth setting. Maybe UMass's or GT's algorithms can be adapted here for handling missing value.***

mDOT RESPONSE: Thank you for this suggestion. Indeed, we are planning to have the students working on imputation work with students on mRisk to incorporate and evaluate its impact.

6. OTHER MISCELLANEOUS COMMENTS

Other Comments
SUN:

- ***I wonder if the data can be shared to the public as they would be valuable resources for research and education in general.***

mDOT RESPONSE: Thank you for this suggestion. As described above, we have publicly released curated and labeled wearable sensor data previously and plan to release new ones as well.

- ***Also, it will be good to summarize the publications related to each research thrust in future.***

mDOT RESPONSE: Thank you for this suggestion. We will list the publications in the TR&D presentations to EAC from here onwards.

mDOT Center Review
from Dr. David Kennedy
Project Period 2 (12/01/2021 – 11/30/2022)

1. OVERALL CENTER STRUCTURE & DIRECTION

Notable Strengths
KENNEDY:

- ***The Center has established a clear set of directions.***

- ***The technology development of the TRDs and the infrastructure provided by the Training are synergizing in a number of areas.***

mDOT RESPONSE: Thank you for your kind words.

Perceived Weaknesses
KENNEDY:
- ***There felt to be one-to-one mapping between the technology developed by the TRDs and a specific target CP for each. Make sure that the use of each of the technologies eventually has a broader use.***

mDOT RESPONSE: Thank you for this very good suggestion. Although we are taking some initiatives in this direction by directly recruiting researchers to use some of the technologies developed in the center (e.g., imputation, stress-triggered prompting, and reinforcement learning toolbox), we are planning to brainstorm with the EAC on how to reach a wider user base in our annual meeting.

Other Comments
KENNEDY:
- ***Target the number of CPs and SPs to be ~10 each by the time of renewal. Some existing CPs and SPs should 'sunset'; make sure to have a story about why and what was (or wasn't) successful.***

mDOT RESPONSE: Thank you for this wonderful suggestion as this provides us with a concrete target to aim for, while taking into account the expiration dates of the current CP's and SP's. Developing a story from the experiences of each CP and SP is a wonderful idea which can help inform our approach for the recruitment of new CP's and SP's as well as improve our approach in how we work with them effectively and efficiently.

- ***Make sure to develop strategic alliances with other initiatives (i.e. European mHealthHUB). The overall 'problem' is bigger than the mDOT Center itself, try to be part of a bigger solution, while maintaining a clear 'this is the piece of the problem WE solve' vision.***

mDOT RESPONSE: Thank you for this great suggestion. We will develop a plan on how to achieve this in Year 3. It should help us become a better contributor to the mHealth community.

- ***Similarly, try to connect in some way to the other network of NIBIB P41's.***

mDOT RESPONSE: Another great timely suggestion. We have started looking into this to identify an initial set of P41's that we can approach to explore relationships.

2. TRAINING & DISSEMINATION STRUCTURE & DIRECTION

<u>Notable Strengths</u>
KENNEDY:

- ***The mHealth Training Institute (mHTI) seemed to be very effective.***

mDOT RESPONSE: Thank you for the assessment.

<u>Perceived Weaknesses</u>
KENNEDY:

- ***How to measure impact of the training. Is there a potential control group from good students not selected?***

- ***Follow-up should be continued beyond 3 months. Knowing what trainees think right after the event is one thing, but 6 month and 1+ year engagement is helpful. What are they following through with, where do they need additional support?***

mDOT RESPONSE: We plan to use the recommendation to develop a matched control group (applicants who were not selected but share similar profiles). We plan to explore the use of the Flight Tracker software to conduct such studies in the future.

We will explore ways to collect 1 year follow-up on mHTI to investigate the long-term effects of the mHTIs.

<u>**Other Comments**</u>
KENNEDY:

- ***What about other engagers (website viewers, tool users, etc.). Is it possible to do metrics and assessments on these type of users (publication citation, user 'happiness')?***

- ***Continue to actively attend to and monitor diversity and equity efforts.***

mDOT RESPONSE: We are currently exploring the features of the Flight Tracker software. A UCLA graduate student (Education & Information Studies) will be working with the mDOT Center's evaluative specialist (Prof. Minjeong Jeon) to develop such metrics and assessments.

The profiles of the mHTI scholars (74% female, 37 % nonwhite) and the disciplinary and geographic distribution of the scholars manifests the effectiveness of the DEI considerations that guide scholar selection. We will continue to augment our efforts in future mHTIs. Also, curating the recorded educational materials for asynchronous access allows broader access by a wide range of researchers interested in the mDOT Center's educational program.

3. mDOT CENTER SOFTWARE

<u>**Notable Strengths**</u>
KENNEDY:

- ***A number of important software tools are planned and in progress; these are designed to embody the technologies developed by the TRDs.***

- ***The Mobile Open Observation of Daily Stressors (MOODS) technology seems well deployed and tested***

mDOT RESPONSE: Thank you for the assessment.

Perceived Weaknesses

KENNEDY:

- ***Continue to think about how to document the utility and impact of the software on the community.***

mDOT RESPONSE: We have just started a new project around mHealth Inferencing from wearable sensors. It is being designed as a public tool which allows researchers, IRBs, or anyone else to input a set of sensors and devices they would like to use data from, and the tool will then provide possible inferences that are possible. These inferences are being derived and scraped from published research papers. This tool will eventually gain a set of risks to participants and provide hints and advice to those working with human subjects. We anticipate hosting the tool on the web where we can track, through analytics, its utilization. For the other tools, we will be looking at adding analytics to them as appropriate to measure utilization.

Other Comments

KENNEDY:

- ***Lots of data is referred to. To better appreciate this data and its impact, parse out the types of data - how much data and from what sources to show what is exactly being supported.***

- ***Similarly, lots of other 'studies' are involved, make sure the breadth of this impact is documented.***

mDOT RESPONSE: Thank you for this great suggestion to quantify and document the impact of the center via the size and diversity of datasets. We believe we can come up with a good story for this. For example, the MOODS study now contains about 750GB of compressed data from a variety of data sources including motion (accelerometer and gyroscope), pulse information (PPG), and computed information (stress likelihoods). The more important piece regarding "lots of data" is that the system architecture and data processing pipelines are built in a way where this data scale is not a concern, and they can produce the AI inferencing needed to support the various projects. We will make clear the precise impact of software on each study as a way to show the broad reach of the tools mDOT produces.

4. ADMINISTRATION STRUCTURE & DIRECTION

Notable Strengths

KENNEDY:

- ***Overall, the administration is accomplishing the necessary management and public-facing aspects of the Center.***

- ***Virtual external review performed, and an in-person event planned.***

- ***Additional social media efforts are underway.***

mDOT RESPONSE: Thank you for your kind words. Your suggestion from Year 1 about rebranding was very helpful and timely. Fortunately, we were able to get this initiative started.

<u>Perceived Weaknesses</u>
KENNEDY:

- ***Attend to the "cost-benefit ratio" of various social media outlets.***

mDOT RESPONSE: Thank you for suggesting this. We had thus been focused on how to customize our usage of different media outlets. We will plan to conduct a cost-benefit analysis that can potentially help other such scientific centers.

- ***Do you use a formal management software of any sort? Reviewers tend to ask this...***

mDOT RESPONSE: We are transitioning out of Jira-Atlassian, looking for one that is more compatible with our structure and process (i.e. one that incorporates Google Docs). We've used Basecamp, TeamWork, and Atlassian in the past to varying degrees of success but haven't found one that suits the Center's needs perfectly yet. We will have one soon though, and look to implement for the upcoming year.

<u>Other Comments</u>
KENNEDY:

- ***Administration seems to be effective and supportive - overall quite impressed with the flexibility and success of the current progress.***

- ***Thinking about how to frame competitive renewal, timing concerns (when to apply for next phase?).***

mDOT RESPONSE: We would love to get your thoughts on how to approach the timing question.

- ***Continue to keep track of your Institutional Support. This is an important leverage point for future funding.***

mDOT RESPONSE: Thank you for pointing this out. We will document the support we have been receiving from the university so we can present a full picture of all five years in our renewal application.

- ***Keep track of the technologies that 'spin off' to the commercial sector. This too is a valuable 'product' of the Center.***

mDOT RESPONSE: Thank you for this suggestion. We have thus far two startups launched by mDOT faculty. We have also partnered with Proctor & Gamble via CP2 on improving their smart toothbrush technology, with Fitbit via CP3 on developing new physical activity interventions, and collaborated with Arm in TR&D3 to improve embedded machine learning. We plan to brainstorm at the annual meeting with the EAC on how to broaden our partnership with the industry.

mDOT Center Review
from Dr. Veena Misra

Project Period 2 (12/01/2021 – 11/30/2022)

1. OVERALL CENTER STRUCTURE & DIRECTION

Notable Strengths
MISRA:

- ***Center continues to be well organized and focused on mHealth interventions***
- ***The team addressed all the concerns brought up last year by the review board***
- ***The addition of the new CP seems to be relevant to support the mDOT mission***
- ***All the TRDs are relevant and address the key challenges***
- ***The specific aims are addressing the key challenges for mDOT***
- ***The presentation was very clear***
- ***Center Director continues to provide strategic leadership of the Center***

mDOT RESPONSE: Thank you for kind words.

Perceived Weaknesses
MISRA:

- ***The fact that several CPs and SPs are ending could lead to some issues regarding resources available to support the CPs and SPs from the customer side.***

mDOT RESPONSE: You are correct about the impending expiration of several current CP’s and SP’s. We are taking a three-pronged approach. First, we plan to continue working with the current set of CP’s and SP’s in their no-cost extension phase and past their expiration to ensure that their needs are met. Second, we are working with our existing collaborators on new collaborative grants (e.g., the new CP8) that align even more closely with the mDOT’s focus on designing, optimizing, and deploying mHealth interventions. Third, we have also begun recruiting a new set of collaborators (some have newly awarded grants, discussion with two such SP’s are currently ongoing and some are submitting new grants) to expand the network of collaborators beyond the initial set of collaborators. We also plan to publicly solicit new CP’s and SP’s via our website, mailing lists, and social media.

- ***The field is even more crowded, and the team should continue to set themselves apart.***

mDOT RESPONSE: Very good observation about the rapid growth in this area of mHealth interventions. We would like to work with our EAC during the annual meeting to develop an overarching long-term vision for mDOT that sets our future work apart, complementary, and highly useful for the mHealth community. The MOODS study software implementing AI models on commercial smartwatched to triggered prompts on smartphones in real-time via widely disseminable app, continuous estimation of composite risk for adverse behavioral events, and RL with participant pooling and network effects to accelerate personalization are some promising recent developments that we plan to build upon in developing our vision.

- ***Role of industry could be enhanced.***

mDOT RESPONSE: Thank you for this suggestion. Thus far, two startups have been launched by mDOT faculty, while two other faculty have taken up roles at the industry. We have also partnered with Proctor & Gamble via CP2 on improving their smart toothbrush technology, with Fitbit via CP3 on developing new physical activity interventions, and collaborated with Arm in TR&D3 to improve embedded machine learning. We plan to brainstorm at the annual meeting with the EAC on how to broaden our partnership with the industry.

2. TR&D3-TRANSLATION STRUCTURE & DIRECTION

Notable Strengths

MISRA:

- ***TR&D3 is well organized and had good progress over the last year***
- ***The three CP projects are addressing the push-pull***
- ***New opportunities for new CPs in lymphedema detection are being explored***
- ***The aims are pushing the technology envelope for edge computing and imaging***
- ***The scalability of the number of wearables is impressive***
- ***Collaboration with TR&D1 on the smoking cessation can further solidify the work in TR&D3***

mDOT RESPONSE: Thank you for your encouraging words. Your technical insights for our TRD is truly appreciated. We hope to strengthen our Push pull relationship with CPs. While we fully believe fluid detection and monitoring will be a new strength for us, our focus will also be on technologies that are readily deployable based on current industry software standards.

Perceived Weaknesses

MISRA:

- ***Connection with SPs was not discussed.***
- ***Some roadmap of TR&D3 technologies could support future opportunities.***

mDOT RESPONSE: Thank you again for your analysis. Admittedly we have been slow in establishing closer relationship with our proposed SPs. This is in part due to the push nature of these relationships that require mature new technologies, which requires initial work to be completed. We hope to build a strategic roadmap for TR&D3 and focus on areas that are closer to provide direct benefits to the CP and SPs.

3. CP RESEARCH: STUDENT WORK (NETWORK OPTIMIZATION) - UCLA

Notable Strengths
MISRA:

- ***Good presentation by the student***
- ***Latency is good and the performance is also good suggesting a good overall approach***

mDOT RESPONSE: Thank you for the encouraging words - we really appreciate it.

Perceived Weaknesses
MISRA:

- ***Current state of the art was not shown for robust inferences***
- ***Also include drawbacks of your approach to present a full picture***

mDOT RESPONSE: You are right on both points - in part this is simply because this aspect of the work (robustness, backward compatibility, etc.) is less mature. We will address both these issues as we progress and in our planned publications.

4. CP RESEARCH: STUDENT WORK (MICROMARKERS) - OHIO STATE

Notable Strengths
MISRA:

- ***Good presentation with good accomplishments***
- ***The approach of compressing the data, producing a generic raw data stream and processing that seems to be an innovative approach***

mDOT RESPONSE: Thank you for your encouraging words. We hope to generalize this approach of generic raw data stream generation to more sensor modalities in future periods of the center.

Perceived Weaknesses

MISRA:

- ***The team could address privacy issues better as the reduced data still appears to preserve patient specific signals***
- ***More analysis on compression ratio and performance is critical***

mDOT RESPONSE: We agree that both of these are areas that require more in depth study. In future work we aim to improve privacy preserving features by including explicitly a discriminator/critic trained to penalize information that will aid to re-identify subjects based on sensor data driving inspiration from training setup of generative adversarial networks. As you point out our compression ratio at this point is controlled by the size of the latent space or the bottleneck. We will explore this and other dimensions such as window size for the sensor data to control the compression ratio and tabulate task specific performance as a function of the compression ratio.

5. RF-BASED NEW DIRECTIONS

<u>**Notable Strengths**</u>

MISRA:

- ***Impressive progress in using RF arrays for imaging***
- ***Good target applications***

mDOT RESPONSE: Thank you for your insights. We believe this a strong growth area for our center, that will also shape the requirements for next generation edge devices in computation and communication.

<u>**Perceived Weaknesses**</u>

MISRA:

- ***Given the limit of the imaging being 10cm, what can you not achieve?***

mDOT RESPONSE: This is a very interesting question that requires more nuanced analysis. The depth of penetration is in fact a frequency-dependent parameter as the conductivity and loss-tangent of the various tissues are frequency-dependent. While 10cm is achievable for low frequencies (e.g 500Mhz) total bandwidth of the backscatter signal at those frequencies is quite limited resulting in lower spatial resolution. Therefore, such as small size features are both possible for all applications. We will study using empirical data and illustrate the depth vs. resolution tradeoff in this modality to provide specific performance metrics for this new sensor modality.

mDOT Center Review
from Dr. Jason Hong

Project Period 2 (12/01/2021 – 11/30/2022)

1. OVERALL CENTER STRUCTURE & DIRECTION

Notable Strengths
HONG:

- ***Diversity of research portfolio (overall) and for privacy specifically is excellent.***
- ***Technical depth of the privacy research is strong.***
- ***Team demonstrates a great deal of thoughtfulness about privacy issues.***

mDOT RESPONSE: Thank you for your kind and encouraging words.

Perceived Weaknesses
HONG:

- ***Team is doing well on the research side of privacy, but needs more on the operational side of privacy where systems are deployed in studies.***
- ***Privacy seems to be siloed in just a few specific projects focused exclusively on privacy.***
- ***Would be useful to consider feedback from participants, as well as healthcare providers, about any potential privacy concerns with the systems being designed and built. Early feedback is better than late feedback, and late feedback is better than no feedback.***

mDOT RESPONSE: Thank you for encouraging us to seek feedback early from stakeholders. Our work currently focuses on research studies with stakeholders being researchers and study participants. Our experience thus far has shown that the privacy issues in this setting is managed largely via IRB protocol and consent forms. But, we do see knowledge gaps (in both researchers and participants) in terms of emerging privacy risks due to growing capabilities of wearable sensors due to development of new AI models. We plan to undertake initiatives in Year 3 that help fill this gap via assisting with appropriate language to be included in IRB protocols. While doing so, we will also collect feedback on other unmet needs of the mHealth research community from a privacy perspective.

2. CENTER PRIVACY STRUCTURE & DIRECTION

Notable Strengths
HONG:

- ***As noted earlier, strong technical depth in the team with respect to privacy.***
- ***Presentations also showed good use of human-centered methods and perspectives on privacy.***

mDOT RESPONSE: Thank you for your kind and encouraging words.

Perceived Weaknesses
HONG:

- ***As noted above, privacy seems to be siloed into just a few research projects.***
- ***Other teams in the Center seem to be lacking guidance on how to address non-research kinds of privacy issues, e.g. data storage, encryption, data deletion, etc.***

mDOT RESPONSE: We agree with this feedback, and while during the preceding year we attempted to engage with the other TR&Ds, we have a long ways to go.

Other Comments
HONG:

- ***Feedback from Q&A suggests that privacy is a secondary concern for research projects in early stages. This is a reasonable response, given the difficulties of building out systems and designing studies. However, may want to consider different tiers for privacy based on the stage of the research. For small-scale and/or early-stage studies, IRB approval alone is likely sufficient. For medium- and large-scale studies as well as more mature studies, should make privacy more central, in terms of design of systems, the study design, data management, getting early feedback from participants and/or healthcare providers before designing and deploying systems, getting feedback during and after the study, etc.***
- ***Consider holding privacy workshops where team members can discuss challenges, best practices, and policies that the entire team may want to adopt (e.g. tiers of privacy based on stage of research).***

mDOT RESPONSE: Thank you for these suggestions about tiering & holding a privacy workshop. We will do both.

3. CP RESEARCH: STUDENT WORK (PRIVACY PERCEPTION) - UCLA

Notable Strengths

HONG:

- ***Good human-centered approach, especially before building any systems.***

- ***Intriguing results, will be good to see next steps and how it might influence a deployment. Could be stronger if tied to a specific initiative / study.***

mDOT RESPONSE: Thank you for the feedback and the encouraging words. We will try to find a specific study to connect to.

Perceived Weaknesses

HONG:

- ***This was one of the questions I asked, how people's perceptions and feelings might change over time. Here is a paper by Leysia Palen that may be relevant, showing that people's initial perceptions of mobile phones don't necessarily match their perceptions after a month of use. Going wireless: behavior & practice of new mobile phone users.***

- ***There are some fundamental tradeoffs with any method used to probe privacy, e.g. surveys might capture what people say vs what they do, or people's attitudes might change over time with acclimation to the tech, etc. As such, may want to complement the work with other methods to probe people's concerns.***

mDOT RESPONSE: We agree on both points - our survey-based approach does limit us to the kind of issues we can probe. We will explore complementing the survey with a deployment-based approach where people "live with" the device for some time. Thanks for the pointer to the Palen paper.

Other Comments

HONG:

- ***Rushil Khurana had a somewhat similar study as the one presented, asking people about their perceptions of privacy under different sensing circumstances and granularities. This was in his dissertation, which for some reason is not yet available online. You may want to ask him or his advisor (Mayank Goel) for a copy. They also told me that they submitted this work to CHI 2023.***

- ***Less related but still useful is this paper by Zheng et al at CSCW: User perceptions of smart home IoT privacy.***

- ***Yet another related paper: Privacy Expectations and Preferences in an IoT World.***

- ***You may want to look at research in HRI (human-robot interaction) about how the shape and form of robots influences people's perceptions. I was thinking that the shape and form of the cameras may affect how people think and feel about them.***

- ***Might want to see if privacy nutrition labels (e.g. An Informative Security and Privacy "Nutrition" Label for Internet of Things Devices) might change people's perceptions.***

mDOT RESPONSE: Thank you for all these valuable pointers - we will follow up.

4. CP RESEARCH: STUDENT WORK (WRIST PRINT) - MEMPHIS

Notable Strengths
HONG:

- ***New kind of reidentification problem with respect to IMU data.***

mDOT RESPONSE: Thank you.

Perceived Weaknesses
HONG:

- ***Better if there were a clearer threat model. For the most part, the data will likely stay on backend. So one possible threat model is re-identification if the data is shared (e.g. with other researchers). If this is the case, need to make that clearer.***

- ***Consider alternative (or additional) metrics. For example, the password community has moved from entropy to number of guesses. Figuring out the right metric is an understated and undervalued kind of research contribution.***

- ***Consider how to tie the research closer to health systems being built and deployed by other research thrusts.***

mDOT RESPONSE: Thank you for these very useful suggestions. We agree about the need to both clarify the threat model and to adopt more useful metrics that reflect the current thinking in the S&P community. We will plan to revise the pitch accordingly for the next paper on this topic. The published WristPrint research largely relates to release of wrist-worn accelerometry data by CP7. But, the next work on timing of steps may also have implications for CP3 that collect steps data and deliver interventions on them if a future iteration decides to collect the timestamp of steps in place of aggregate step count.

Other Comments
HONG:

- ***Is it possible to generalize the work for other kinds of streaming sensor data? Are there general patterns for certain classes of sensor data?***

mDOT RESPONSE: This is a very good question. Biometric properties of physiological data (such as ECG and heart rhythm) is well-established. WristPrint established that motion data also has re-identification potential. But, it did not provide a generalized theory that can be applied to other kinds of wearable sensor data. In the next work, our goal will be to explore how generalizable is the new approach to different kinds and granularities of wearable sensor data.

5. FUTURE PLANS

Notable Strengths
HONG:

- ***Continuing the existing lines of work will be a useful and valuable contribution to the community with respect to privacy.***

- ***Holding some kind of workshop to discuss issues of privacy has good potential for making a positive impact.***

mDOT RESPONSE: Thank you for the encouragement and the suggestion about the workshop, which we will act on.

mDOT Center Review
from Dr. David Mohr
Project Period 2 (12/01/2021 – 11/30/2022)

1. OVERALL CENTER STRUCTURE & DIRECTION

Notable Strengths
MOHR:

- ***An impressive scope, spanning intervention discovery to translation into intervention of digital interventions.***

- ***The matrix of TR&Ds and functions makes sense – particularly both the supports and products.***

mDOT RESPONSE: Thank you for your encouraging words.

Perceived Weaknesses
MOHR:

- ***I don't see any weaknesses. More as I reflect on our discussion, I have questions that I didn't raise. So I'll mention a few here just as considerations.***

- ***One thing we did not talk much about, but which I should have asked more about, are plans for sustainment. It seems to me that there are lots of tools out there that are potentially useful, but nobody uses or knows about. I'm sure you've thought about this, but I know in the frenzy of work during a grant, these around sustainment can be deprioritized. But to the extent your goals include have infrastructure and services that can be sustained after the expiration of funding, it could be useful early on to identify potential users, learn their needs and importantly limitations, how they learn about and access such tools – essentially sort of user centered design.***

mDOT RESPONSE: Very good suggestions. In Year 2, we undertook a wide variety of branding and dissemination tasks, triggered by suggestions from another EAC member (Dr. David Kennedy). We hired a staff member to undertake these activities. We also began working on developing tools (from research conducted in Years 1 and 2) that are easily usable by the wider community. Both of these position us well to realize the goal you have laid out about getting our research disseminated to a broader community in the form of tools.

For sustainment, the P41 mechanism allows for two 5-year renewals, which if successful provides a longer time window to have an impact on the scientific community via adoption of our methods and tools.

MOHR:

- ***If I remember correctly your projects are exclusively with outside funded projects. It seems that could pose potential challenges in aligning the aims of the outside investigators and the mDOT teams, especially given I'd expect, even if the mDOT Center is providing substantive value, it also might entail additional processes and planning that may not have been considered in budgets and organizations. And I'm sure there are other challenges. These potential problems are mitigated somewhat, since it seems most or all of the outside researchers are close collaborators of mDOT Center investigators. Problems also present opportunities. If the goal of the mDOT Center is produce infrastructure and services that are sustainable beyond this funding, tracking and monitoring those processes may be useful. We are currently doing this in our Center through periodic semi-structured interviews (again, sort of UCD) with key stakeholders in all organizations involved, which has been useful in recognizing where problems exist, where our overarching frameworks can be tweaked and improved.***

mDOT RESPONSE:

- Thank you for these suggestions. We indeed plan on undertaking the kind of active feedback solicitation via focus groups, surveys, and interviews once our tools are ready for dissemination. We also plan to track the usage or adoption of our code from open-source GitHUB repositories.

2. REAL-TIME LEARNING & PERSONALIZATION BY REINFORCEMENT LEARNING

Notable Strengths

MOHR:

- ***If I understood correctly, the aims of optimizing personalization methods, reducing the amount of time required, by using group-level data and accounting for treatment effects that are delayed (essentially managing different time scales across sensed data and outcomes). These are really critical issues (ones we deal with in mental health, where outcomes can occur weeks after sensed activity).***

- ***The goal of using data collected in MRT designs to produce JITAIs (in the process of the MRT project) could be an accelerator for this area of research. We have one project in our Center that would directly benefit from such methods.***

- ***Building a toolbox could be a significant benefit to researchers, and possibly the digital health industry as these interventions make their way into practice.***

mDOT RESPONSE: Thank you for the encouragement! 2a is particularly challenging. We are making some progress in this area and aim to report on this next year.

Perceived Weaknesses

MOHR:

- ***I don't have any significant comments or suggestions for this project. Thinking of this as a potential user, I have some questions about the kind of data we deal with in mental health. Unlike step counts, smoking, or cleaning teeth, some (but not all) of our treatment targets are less concrete – like mood. This is typically measured with EMA or PROs, and thus suffer from issues of reliability. Other markers, such as sensed sleep markers (sleep onset and offset) also are usually messier, particularly when extracted from devices not designed to measure those features, such as phone sensor data. So one of the questions I would have as a potential user is how to manage JITAIs with these messier, less reliable data, which are more common in mental health.***

mDOT RESPONSE: We agree that in many mobile health applications there are treatment targets that are difficult to measure such as mood, salience of physical activity and self-efficacy. Longer term our goal is to view these targeted outcomes as latent time-varying constructs. We will have access to multiple observations related to these latent constructs (both sensor and as well as occasional self-report). These observations can be used to construct predictors as well as measures of confidence in these predictors. At least three exciting areas of research are related to this effort. The first is to develop algorithms that will prompt for self-report, only when this self-report will be useful to improve the measure of confidence. The second area is how we might develop algorithms that make use of the measures of confidence in order to determine when and which treatment should be provided (this second area is related to 3. below). A third is how the algorithm might make use of more intermediate outcomes (in addition to proximal outcomes) in order to speed up learning. Further in our collaborations with behavioral scientists we are encouraging them to frame some of the content of the behavioral treatments according to how confident we are in the prediction.

B.4. What opportunities for training and professional development has the project provided?

All personnel working on the project learn about their own domains and collaborating domains via regular communication and collaborative research activities. In addition, they learn critical team science skills via the interdisciplinary collaborations among the investigative teams as well as by working closely with the health research team from our collaborative projects (CP). They get unique opportunities to test their ideas out by developing working software, getting regular feedback from CP investigators and their staff, and then get to test their work in real-life deployment. All personnel also learn communication skills via regular presentations and discussions. Finally, they attend relevant conferences and professional meetings to communicate and network with other members of their research community.

Training in Professional Software Development - The software is designed to be extensible and usable by a variety of researchers including students and postdocs. Students who wish to contribute to the software platform reach out to the software team and we start a discussion to determine how we can best help each other. In general, this process includes the utilization of our repositories on GitHub for managing the software and Pivotal Tracker for handling bug reports and project planning.

Learning from Group Meetings - Minutes of teleconference calls as well as audio recordings are available for review by all team members. They help capture the content and context of discussions among mDOT Center team members and enable the team to keep up with what is going on outside their particular area of research. These are archived on the mDOT Center Google Drive which allow for easy access to information in a usable and consumable manner.

mHealth Awareness via mHealthHUB - The mHealthHUB website serves as a location where students and staff, as well as the general public, can find mHealth news aggregated. It includes a calendar of events, which also features submission deadlines for pertinent conferences and announcements of mDOT Center webinars. https://mhealth.md2k.org/

Sharing Publications - mDOT Center investigators have published or have submitted and under review 38 papers related to mDOT Center research. The papers have been readily available for team review to facilitate broader discussion.

Webinars - We have an archive of over 32 webinars and over 22 hours of training video content. Students and staff are encouraged to attend live, and webinars are posted to the mDOT Center YouTube channel and links are featured on the mHealthHUB. https://www.youtube.com/c/mdotcenter

Multidisciplinary Training - Each mDOT Center-affiliated graduate student has a faculty advisor to guide them in their studies and they get to work closely with students and investigators at other sites as well as from collaborative projects. This way, they learn to work in multidisciplinary teams.

mHealth Training Institute Lectures - All the presentations by the mHTI faculty are archived on mHealthHUB that mDOT personnel can watch at their convenience https://mhealth.md2k.org/mhealth-training-institute

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Ho E, Jeon M, Lee M, Luo J, Pfammatter AF, Shetty V, Spring B. Fostering interdisciplinary collaboration: A longitudinal social network analysis of the NIH mHealth Training Institutes. Journal of clinical and translational science. 2021;5(1):e191. PubMed PMID: 34849265; PubMed Central PMCID: PMC8596066; DOI: 10.1017/cts.2021.859.
In Process at NIHMS	Liu R, Garcia L, Srivastava M. Aerogel: Lightweight Access Control Framework for WebAssembly-Based Bare-Metal IoT Devices. IEEE/ACM Symposium on Edge Computing. 2021 December:94. DOI: 10.1145/3453142.3491282.
Complete	Saghafian S, Murphy SA. Innovative Health Care Delivery: The Scientific and Regulatory Challenges in Designing mHealth Interventions. NAM perspectives. 2021;2021. PubMed PMID: 34611601; PubMed Central PMCID: PMC8486421; DOI: 10.31478/202108b.
In Process at NIHMS	Saleheen N, Ullah MA, Chakraborty S, Ones DS, Srivastava M, Kumar S. WristPrint: Characterizing User Re-identification Risks from Wrist-worn Accelerometry Data. ACM SIGSAC Conference on Computer and Communications Security. 2021 November 13:2807. DOI: 10.1145/3460120.3484799.
Complete	Yao J, Brunskill E, Pan W, Murphy S, Doshi-Velez F. Power Constrained Bandits. Proceedings of machine learning research. 2021 August;149:209-259. PubMed PMID: 34927078; PubMed Central PMCID: PMC8675738.
Complete	Qian T, Yoo H, Klasnja P, Almirall D, Murphy SA. Estimating time-varying causal excursion effect in mobile health with binary outcomes. Biometrika. 2021 September;108(3):507-527. PubMed PMID: 34629476; PubMed Central PMCID: PMC8494142; DOI: 10.1093/biomet/asaa070.
Complete	Psihogios AM, Rabbi M, Ahmed A, McKelvey ER, Li Y, Laurenceau JP, Hunger SP, Fleisher L, Pai AL, Schwartz LA, Murphy SA, Barakat LP. Understanding Adolescent and Young Adult 6-Mercaptopurine Adherence and mHealth Engagement During Cancer Treatment: Protocol for Ecological Momentary Assessment. JMIR research protocols. 2021 October 22;10(10):e32789. PubMed PMID: 34677129; PubMed Central PMCID: PMC8571686; DOI: 10.2196/32789.
Complete	Zhang KW, Janson L, Murphy SA. Statistical Inference with M-Estimators on Adaptively Collected Data. Advances in neural information processing systems. 2021 December;34:7460-7471. PubMed PMID: 35757490; PubMed Central PMCID: PMC9232184.
In Process at NIHMS	Civek BC, Ertin E. Bayesian Sparse Blind Deconvolution Using MCMC Methods Based on Normal-Inverse-Gamma Prior. IEEE transactions on signal processing : a publication of the IEEE Signal Processing Society. 2022 March 03;70:1256. DOI: 10.1109/TSP.2022.3155877.
N/A: Not Journal	Civek BC, Ertin E. MCMC Methods for Estimation of Thoracic Fluid Levels using UWB Radar. [Poster]. Ioannina, Greece: IEEE BHI-BSN; 2022 September 30. Available from: https://bhi-

	bsn-2022.org/.
In Process at NIHMS	Saha SS, Sandha SS, Garcia LA, Srivastava M. TinyOdom: Hardware-Aware Efficient Neural Inertial Navigation. Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies. 2022 July;6(2):1. DOI: 10.1145/3534594.
In Process at NIHMS	Saha SS, Sandha SS, Pei S, Jain V, Wang Z, Li Y, Sarker A, Srivastava M. Auritus: An Open-Source Optimization Toolkit for Training and Development of Human Movement Models and Filters Using Earables. Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies. 2022 July;6(2):1. DOI: 10.1145/3534586.
N/A: Not Journal	Saha SS. THIN-Bayes: Platform-Aware Machine Learning for Low-End IoT Devices. [Poster]. San Francisco, CA: tinyML Summit 2022; 2022 March 30. Available from: https://cms.tinyml.org/wp-content/uploads/talks2022/Saha-S.-Sayan-SW-tools.pdf.
In Process at NIHMS	Ullah MA, Chatterjee S, Fagundes CP, Lam C, Nahum-Shani I, Rehg JM, Wetter DW, Kumar S. mRisk: Continuous Risk Estimation for Smoking Lapse from Noisy Sensor Data with Incomplete and Positive-Only Labels. Proceedings of the ACM on interactive, mobile, wearable and ubiquitous technologies. 2022 September 07;6(3):1.
Complete	Qian T, Walton AE, Collins LM, Klasnja P, Lanza ST, Nahum-Shani I, Rabbi M, Russell MA, Walton MA, Yoo H, Murphy SA. The microrandomized trial for developing digital interventions: Experimental design and data analysis considerations. Psychological methods. 2022 January 13. PubMed PMID: 35025583; PubMed Central PMCID: PMC9276848; DOI: 10.1037/met0000283.
Complete	Nahum-Shani I, Shaw SD, Carpenter SM, Murphy SA, Yoon C. Engagement in digital interventions. The American psychologist. 2022 March 17. PubMed PMID: 35298199; PubMed Central PMCID: PMC9481750; DOI: 10.1037/amp0000983.
In Process at NIHMS	Coppersmith DDL, Dempsey W, Kleiman EM, Bentley KH, Murphy SA, Nock MK. Just-in-Time Adaptive Interventions for Suicide Prevention: Promise, Challenges, and Future Directions. Psychiatry. 2022 July 18:1-17. PubMed PMID: 35848800; DOI: 10.1080/00332747.2022.2092828.
PMC Journal - In process	Lee MH. Dynamics between mHealth scholars’ communication networks and team psychological safety: Analysis with actor-oriented social network models. PLOS One. Forthcoming.
In Process at NIHMS	Xu MA, Moreno A, Nagesh S, Aydemir VB, Wetter D, Kumar S, Rehg JM. PulseImpute: A Novel Benchmark Task for Pulsative Physiological Signal Imputation. Conference on Neural Information Processing Systems (NeurIPS). Forthcoming:2022.
In Process at NIHMS	Data-driven Interpretable Policy Construction for Personalized Mobile Health. IEEE ICDH.
In Process at NIHMS	Designing Reinforcement Learning Algorithms for Digital Interventions: Pre-Implementation Guidelines. Algorithms.
In Process at NIHMS	Heteroscedastic Temporal Variational Autoencoder For Irregularly Sampled Time Series. International Conference on Learning Representations.
In Process at NIHMS	Batch policy learning in average reward Markov decision processes. Annals of statistics.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Category	Explanation

Data or Databases , Research Material , Audio or video	https://mhealth.md2k.org/
Audio or video	https://www.tiktok.com/@mdotcenter
Audio or video	https://www.youtube.com/c/mdotcenter
Educational aids or curricula	https://github.com/nesl/hide-and-seek-challenge
Other	https://twitter.com/mdot_center
Other	https://www.linkedin.com/in/mdotcenter/
Other	https://mdotcenter.org/
Other	https://mhti.md2k.org/
Other	https://www.reddit.com/user/mDOT_Center/
Other	https://md2k.org
Other	http://mprov.md2k.org/
Other	http://mperf.md2k.org/
Other	https://mguard.md2k.org/
Research Material	https://github.com/nesl/auritus
Software	https://github.com/MD2Korg/
Software	https://github.com/mDOT-Center/
Software	https://github.com/SENSE-Lab-OSU/MotionSenseHRV_v3
Software	https://github.com/nesl/tinyodom
Software	https://github.com/MD2Korg/wrist-print
Software	https://github.com/reml-lab/hetvae
Software	https://github.com/reml-lab/BayesLDM

C.3 TECHNOLOGIES OR TECHNIQUES

Category	Explanation
Instruments or equipment	MotionSense HRV: we have developed a dual-core version of our wristband and rewrote the software stack from the ground up to support common machine learning abstractions often encountered in bio/micromarker implementations. We performed detailed analysis on techniques for optimizing the model and memory utilization of the deployed model in the system. The firmware was further modified to be backward compatible with the previous version of the firmware by modifying the packet format used in data transfer. The activity-related measure termed ENMO (Euclidean norm minus one) is also implemented on the sensor firmware, which serves as a measure for activity level.

Models	BayesLDM: A toolbox for the specification and estimation of mechanistic models in the dynamic bayesian network family. This toolbox focuses on making it easier to specify probabilistic dynamical models for time series data and to perform Bayesian inference and imputation in the specified model given incomplete data as input.
Software	Heteroscedastic Temporal Variational Autoencoder for Irregularly Sampled Time Series (HetVAE): HeTVAE is a deep learning framework for probabilistic interpolation of irregularly sampled or sparse time series data.
Software	Mobile Open Observation of Daily Stressors (MOODS): The MOODS software gained a variety of feature additions and bug fixes during the active study as previously described. The smartwatch app had a single new feature that improved the software stability and functionality when the watch's battery was fully depleted and the device ran out of power. Additionally, 5 bugs were found and fixed. The most recent update to the app occurred on December 21, 2021. The smartphone app received significantly more enhancements and bug fixes during this period. Its enhancements include a Just-In-Time annotation process, participant notification preferences, logging of system behaviors for data diagnostics and system debugging on participant devices, the ability to determine internet connectivity and show appropriate UIs when the servers are unavailable, and predictive location names and stress annotations to aid participant inputs. During this same interval, 15 bugs were identified and fixed with the most recent occurring on March 8, 2022. All enhancement and bug fixes were immediately pushed to participants through their respective app stores after internal testing was completed. This resulted in 10 unique software releases for the smartphone app during this period. The MOODS cloud platform received an enhancement that added better annotation capabilities to support new app functionality. Additionally, it received a new feature that allowed the computation of participant stress likelihood bin thresholds necessary for the implementation of the new JIT algorithm. The platform also had 7 bugs identified and resolved in this period.

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Component(s)	Country	SS
SKUMAR4	Y	Kumar, Santosh	PHD	PD/PI	0.0	2.3	0.8		Admin-7221 (mDOT Administrative Core), Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
ERTIN01	Y	Ertin, Emre	PHD	Co-Investigator	0.0	0.9	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
BMARLIN	Y	Marlin, Benjamin M.	PhD	Co-Investigator	0.0	0.5	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SAMURPHY	Y	MURPHY, SUSAN A	PHD	Co-Investigator	1.2	0.0	0.0		Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SHETTY2	Y	SHETTY, VIVEK	DOTH,DDS	Co-Investigator	1.0	0.0	0.0		Tech-7225 (mDOT Training and Dissemination)		NA
HYLAI1	N	Lai, Hsin-Yu	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	2.0	0.0	0.0		Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
ATRELLA	N	Trella, Anna Li	BS	Graduate Student (research assistant)	3.0	0.0	0.0		Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
JINGYIGAN	N	Gan, Jingyi	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
YONGYIGUO	N	Guo, Yongyi	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
SRATHNAM	N	Rathnam,	AB,MS	Graduate	1.0	0.0	0.0		Project-7223 (mDOT		NA

		Sarah		Student (research assistant)					TR&D2 (Optimization):…ment Learning)		
JEONMJ	N	Jeon, Minjeong	PhD	Consultant	1.0	0.0	0.0		Tech-7225 (mDOT Training and Dissemination)		NA
JWBGGERS	N	Biggers, Joseph	MS	Operations Director	2.0	0.0	0.0		Admin-7221 (mDOT Administrative Core)		NA
TWHNAT	N	Hnat, Timothy	BS,OTH,PHD	Staff scientist (Doctoral level)	2.0	0.0	0.0		Admin-7221 (mDOT Administrative Core), Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-7223 (mDOT TR&D2 (Optimization):…ment Learning), Project-7224 (mDOT TR&D3 (Translation): …plementations), Tech-7225 (mDOT Training and Dissemination)		NA
LDRUSH1	N	Tran, Lyndsey		Training Specialist	6.0	0.0	0.0		Tech-7225 (mDOT Training and Dissemination)		NA
SSAMIEI	N	Samiei, Shahin		Research Coordinator	2.4	0.0	0.0		Admin-7221 (mDOT Administrative Core)		NA
HUIWEI123	N	Wei, Hui	BS,MS,PHD	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
VAYDEMIR	N	Aydemir, Varol Burak	PHD,BS	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.0	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
J.REHG	Y	Rehg, James M.	PHD	Co-Investigator	0.3	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
SNAGESH	N	Nagesh, Supriya	BS,PHD	Graduate Student (research assistant)	1.0	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
AFMORENO	N	Moreno, Alexander	BA,MS	Graduate Student (research assistant)	4.5	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
SWAPNILSAHA	N	Saha, Swapnil Sayan	BS,MS,PHD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	2.0	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA

BRIANWANG	N	Wang, Brian		Graduate Student (research assistant)	2.0	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
AKASHSINGH1	N	Singh, Akash Deep	MS,PHD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	1.5	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
NSUGAVANAM	N	Sugavanam, Nithin	BS,PHD	Sr. Research Engineer	1.0	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
SATYASHUKLA	N	Shukla, Satya		Graduate Student (research assistant)	3.5	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
SUSOBHANGHOSH	N	Ghosh, Susobhan	MS,BS	Graduate Student (research assistant)	2.0	0.0	0.0		Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
AZIMULLAH	N	Ullah, Md Azim	BS	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics), Project-7223 (mDOT TR&D2 (Optimization):…ment Learning)		NA
YUYI_CHANG	N	Chang, Yuyi		Graduate Student (research assistant)	6.0	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
TUSHAR_AGARWAL	N	Agarwal, Tushar	BS	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
SRIVASTAVA2	Y	Srivastava, Mani	PHD,MS,OTH	Co-Investigator	0.0	0.0	0.5		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA
MXU870	N	Xu, Maxwell	Ph.D.	Graduate Student (research assistant)	8.0	0.0	0.0		Project-7222 (mDOT TR&D1 (Discovery) - E…Risk Dynamics)		NA
SOUMOBRATA_GHOSH	N	Ghosh, Soumobrata	Ph.D.	Graduate Student (research assistant)	6.0	0.0	0.0		Project-7224 (mDOT TR&D3 (Translation): …plementations)		NA

Glossary of acronyms:
S/K - Senior/Key
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RS - Reentry Supplement
DS - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

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D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

No

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Sub-Project ID	Study ID	Study Title	Delayed Onset	Clinical Trial	NCT	NIH-Defined Phase 3	ACT
Project-002	330869	TR&D2: Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning	YES	NO			
Project-001	330867	TR&D1: Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized	YES	NO			
Project-003	330868	TR&D3: Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations	YES	NO			

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

Yes

Yongyi Guo - YONGYIGUO (9/22); Susobhan Ghosh - SUSOBHANGHOSH (8/22); Jingyi Gan - JINGYIGAN (8/22)
CITI Social and Behavioral Responsible Conduct of Research - This course is for investigators, staff, and students with an interest or focus in Social and Behavioral research. This course contains text, embedded case studies and quizzes.
CITI Social & Behavioral Research Investigators - A course about Unanticipated Problems and Reporting Requirements in Social and Behavioral Research, History and Ethical Principles, The Federal Regulations, Assessing Risk, Informed Consent, & Privacy and Confidentiality
CITI Information Privacy Security (IPS) - IPS covers the principles of data protection, focusing on the healthcare-related privacy and information security requirements of the Health Insurance Portability and Accountability Act (HIPAA) and the educational records and data-related requirements of the Family Educational Rights and Privacy Act (FERPA).

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name	UEI	Congressional District	Address
Primary: UNIVERSITY OF MEMPHIS	F2VSMAKDH8Z7	TN-009	UNIVERSITY OF MEMPHIS ADMINISTRATION 315 MEMPHIS, TN 381520001
Georgia Tech Research Corporation	EMW9FC8J3HN4	GA-005	926 Dalney Street NW Atlanta, GA 30318
President and Fellows of Harvard College	LN53LCFJFL45	MA-005	1033 Massachusetts Avenue, 5th Floor Cambridge, MA 02138
The Ohio State University	DLWBSLWAJWR1	OH-003	1960 Kenny Road Columbus, OH 43210
The Regents of the University of California, San Francisco	KMH5K9V7S518	CA-012	3333 California Street, Suite 315 San Francisco, CA 94143
The Regents of the	RN64EPNH8JC6	CA-033	10889 Wilshire Blvd

University of California			Suite 700, Box 951406 Los Angeles, CA 90095
University of Massachusetts Amherst	VGJHK59NMPK9	MA-002	101 University Drive, Suite B6 Amherst, MA 01002

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period? No

G.12 F&A COSTS

Not Applicable

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
330869	TR&D2: Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning	No	TRD2_Justification.pdf

Project Lead: Murphy, Susan Primary Investigator: Kumar, Santosh

Justification

TR&D2 will provide technology and support to active human subjects studies but will not be conducting research activities involving interaction with living human subjects. All TR&D2 activities involving human subjects data for research will be governed or otherwise overseen by Institutional Review Board (IRB) oversight, as appropriate. Each project that involves human subjects interactions for research or interaction with human subjects data for research will continue to follow the letter and the spirit of regulations protecting the rights and welfare of human subjects in research studies. All interactions with human subjects and/or their data are governed by both internal TR&D2 and institutional policies requiring Institutional Review Board oversight, exemption, or determination that human subjects research is not taking place. Any data involving human subjects collected in TR&D2 projects (e.g., via the CPs and SPs) will be governed by the data management plans of the respective projects. In addition, all human subject data collection will have explicit Institutional Review Board (IRB) approval. It is not known at this time, what human subject data will be collected using TR&D2 technologies, hosted by TR&D2, and used for technology development and testing by TR&D2.

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
330867	TR&D1: Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized	No	TRD1_Justification.pdf

Project Lead: Rehg, Jim   Primary Investigator: Kumar, Santosh

Justification

TR&D1 will provide technology and support to active human subjects studies but will not be conducting research activities involving interaction with living human subjects. All TR&D1 activities involving human subjects data for research will be governed or otherwise overseen by Institutional Review Board (IRB) oversight, as appropriate. Each project that involves human subjects interactions for research or interaction with human subjects data for research will continue to follow the letter and the spirit of regulations protecting the rights and welfare of human subjects in research studies. All interactions with human subjects and/or their data are governed by both internal TR&D1 and institutional policies requiring Institutional Review Board oversight, exemption, or determination that human subjects research is not taking place. Any data involving human subjects collected in TR&D1 projects (e.g., via the CPs and SPs) will be governed by the data management plans of the respective projects. In addition, all human subject data collection will have explicit Institutional Review Board (IRB) approval. It is not known at this time, what human subject data will be collected using TR&D1 technologies, hosted by TR&D1, and used for technology development and testing by TR&D1.

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
330868	TR&D3: Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations	No	TRD3_Justification.pdf

Project Lead: Ertin, Emre

Primary Investigator: Kumar, Santosh

Justification

TR&D3 will provide technology and support to active human subjects studies but will not be conducting research activities involving interaction with living human subjects. All TR&D3 activities involving human subjects data for research will be governed or otherwise overseen by Institutional Review Board (IRB) oversight, as appropriate. Each project that involves human subjects interactions for research or interaction with human subjects data for research will continue to follow the letter and the spirit of regulations protecting the rights and welfare of human subjects in research studies. All interactions with human subjects and/or their data are governed by both internal TR&D3 and institutional policies requiring Institutional Review Board oversight, exemption, or determination that human subjects research is not taking place. Any data involving human subjects collected in TR&D3 projects (e.g., via the CPs and SPs) will be governed by the data management plans of the respective projects. In addition, all human subject data collection will have explicit Institutional Review Board (IRB) approval. It is not known at this time, what human subject data will be collected using TR&D3 technologies, hosted by TR&D3, and used for technology development and testing by TR&D3.

A. COMPONENT COVER PAGE

Project Title: mDOT Administrative Core
Component Project Lead Information: Kumar, Santosh

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will enable a new paradigm of temporally-precise medicine to maintain health and manage the growing burden of chronic diseases. The mDOT Center will develop and disseminate the methods, tools, and infrastructure necessary for researchers to pursue the discovery, optimization and translation of temporally-precise mHealth interventions. Such interventions, when dynamically personalized to the moment-to-moment biopsychosocial-environmental context of each individual, will precipitate a much-needed transformation in healthcare by enabling patients to initiate and sustain the healthy lifestyle choices necessary for directly managing, treating, and in some cases even preventing the development of medical conditions. Organized around three Technology Research & Development (TR&D) projects, mDOT represents a unique national resource that will develop multiple technological innovations and support their translation into research and
practice by the mHealth community in the form of easily deployable wearables, apps for wearables and smartphones, and a companion mHealth cloud system, all open-source.

To execute its research, development, collaboration, training, and dissemination goals, the mDOT Center builds on central operations infrastructure developed through successful administration of the NIH Center of Excellence for Mobile Sensor Data-to-Knowledge (MD2K). MD2K involves 70 investigators, students, postdoctoral fellows, software engineers, and administrative staff, distributed across 13 universities. In addition, MD2K leads or participates in 13 concurrently active research grants from NIH, NSF, and other federal agencies. the mDOT Center takes advantage of an experienced, multidisciplinary team of investigators and technical staff from MD2K. This expertise includes program operations, business management, data management, marketing and communication, study coordination, training coordination, and outreach. The overall goal is to implement an operational structure that facilitates the discovery, optimization, and translation of temporally-precise mHealth interventions to advance health research and improve health outcomes.

The mDOT Center is organized into an Administration Core, a Technology, Training and Dissemination Core (TT&D) and three Technology Research and Development (TR&D) Projects: TR&D1 (Intervention Discovery); TR&D2 (Intervention Optimization), and TR&D3 (Intervention Translation). PI/PD Kumar will serve as the mDOT Center Director, responsible for overseeing all project related activities and will also lead the Administration Core. He will work with an Executive Committee, mDOT Center Operations Office, and External Advisory Committee to carry out this role. The Administration Core will facilitate interactions among the TR&D Researchers and their external collaborators from collaborating and service projects; coordinate the activities of the TT&D Core to enable both targeted and broad-based training and dissemination of methods, tools, and research findings developed through mDOT Center activities; assess the productivity and impact of Center activities; and provide ongoing management, oversight, and planning related to Center funds, resources, and operations. Drawing on its prior leadership experience on the NIH-funded MD2K National Center of Excellence, the Administration Core will provide the managerial and operational structures through which the mDOT Center will achieve its research, development, collaboration, training, and dissemination goals. The Administration Core has five specific aims:

Aim 1: Establish an organizational structure, coordinating procedures, and managerial practices that effectively facilitate coordination, communication, and collaboration among team members, collaborative and service projects, and the broader research community.

Aim 2: Establish operating procedures to successfully work with collaborative projects (CPs) and service projects (SPs), including criteria and mechanisms to receive, review, approve, and facilitate use of mDOT Center resources by CPs and SPs, and establish criteria for prioritizing and selecting CPs and SPs.

Aim 3: Recruit, assemble, and manage an external advisory committee (EAC) of eminent scholars with diverse and complementary expertise to obtain feedback and guidance on research directions, software development, selection of CPs and SPs, as well in the overall structure and operations of the mDOT Center.

Aim 4: Acquire, manage, and leverage institutional support to successfully accomplish the goals of the mDOT Center.

Aim 5: Develop quantifiable measures and implement systems to monitor, assess, and evaluate the quality and utility of mDOT Center products, and continuously improve the long-term impact of Center activities on biomedical research by systematically securing feedback from collaborators and community stakeholders.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We published articles in peer-reviewed international conferences and journals and book chapters. We disseminated information using our websites and social media. Work was also disseminated directly via the following presentations, several of which are archived at mHealthHUB for broader dissemination.

Software and Documentation availability: https://github.com/mDOT-Center/
Each software component produced under the umbrella of the mDOT Center is contained in one or more repositories in our organization's GitHub site. Projects not only contain their source code but any relevant developer documentation and basic tutorials via a README file with additional information in the project's wiki. Many of the projects are anticipated to be released under the BSD-2 open source licensing to allow for others to freely incorporate them into their projects along with us accepting contributions from the greater scientific community back into the projects. The mHealth Hub will contain references to both the mDOT software products along with other relevant community projects.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Software
pJITAI Software (in Collaboration with CP3)
The pJITAI platform is slated to be completed during this next year and be tested as part of an mHealth-based behavioral study. Currently, a user-study with behavioral scientists is underway to test the user interfaces that have been designed. Once this study is complete & the interfaces finalized, these will be incorporated into the pJITAI web interface. We are currently iterating on the Thompson Sampling algorithm's implementation to ensure that it is implemented in the most efficient and straightforward method since we would like this to become a template for others to utilize when building new algorithms. We anticipate having a fully functional system by the end of 2022 when we can hand off the platform to our CP partner for pilot testing & ultimately a full field study deployment. The mDOT team will continue to refine & adjust the software based on our experience with this real-world trial. By the end of this year's reporting period, we would like to have this software near completion & make it available to anyone wishing to utilize the technology or to enhance it with their own algorithms.

Expand mDOT-MIND to Smoking Cessation Interventions (mRisk)
We will build the mRisk modules to expand the capabilities and potential utility of mDOT-MIND framework for smoking cessation intervention research. In addition to detecting stress in real-time, the smartwatch app will include new AI-based models to detect smoking events. The smartwatch model will include a new capability to estimate the risk of a smoking lapse continuously in newly abstinent smokers. We are currently working on building these models based on other MD2K-based data sets before transitioning them into a format suitable for deployment on a smartwatch-based platform. The smartwatch platform will be complemented with additional modules on the smartphone when data aggregations are necessary. During this year, we plan to recruit new collaborative projects based on this platform in order to refine and test the implementation under real-world conditions.

mHealth Ethics Awareness Research Toolkit (mHEART) for mHealth Privacy Awareness
The team is also working on a new mHealth risk assessment tool to help researchers understand the risks & challenges associated with utilizing mobile sensors (e.g. accelerometer, gyroscope, PPG) in human subjects research. This tool will aid those researchers by providing them feedback and information regarding the risks to their subjects based on those risks that have been published by the greater research community. Our vision is to ultimately incorporate an IRB protocol analysis tool that can determine what researchers are utilizing & provide annotations and suggestions to their protocols to address the known risks. In this first year, we will provide a web-based solution that allows researchers to select the platforms & specific sensors they are going to utilize in a study & our tool will provide reference text describing the associated risks & mitigating strategies that are necessary to properly protect the human subjects. This tool will be made available through the mDOT Center's website as a resource available to any researcher to utilize. It will be continuously updated with the latest research as well as incorporating new features as we build them.

Center Operations and Support
The Admin Core will continue to provide administrative, managerial, and infrastructure support to enable the mDOT Center to accomplish its Year 3 goals in research, training, and dissemination activities. In addition to continuing its successful strategies for communication and management, the mDOT Center plans to do several activities in Year 3 tied to the Administration Core Aims:

Aim 1 - Administratively Manage The Center
Annual Meeting: The mDOT Center will look to host its next annual meeting with all Center investigators in attendance.
Student Exchange: The mDOT Center will continue to facilitate and enhance scholar exchanges between subsites/CPs/SPs as possible (virtually or in-person).
Website: The Admin Core will look to expand the utility of the mDOT Center website by redesigning it with the goal to provide informative updates about new publications, software resources, & current center progress.
Award: The administration team will again look to receive, process, & execute all grant subcontracts for the Year 3 award and provide assistance to collaborating institutions with their process.
Renewal: The mDOT Center will begin to prepare for award renewal by updating its 15-year Center vision.

Aim 2 - CP and SP Coordination & Expansion
Expansion: The mDOT Center team intends to expand the number of CPs and SPs and onboard new CPs and SPs as needed.
Facilitate: The mDOT Center administration team will continue to coordinate relevant CP and SP meetings tailored to the push/pull relationship and research.

Aim 3 - Executive Advisory Committee Engagement
Evaluate: The mDOT Center will look to convene the Executive Advisory Committee for its annual evaluation meeting(s) to review the current progress & future direction of the mDOT Center. The EAC's formal reviews will be included in the Year 3 RPPR.
Integrate: The mDOT Center will look to enhance its engagement with the Executive Advisory Committee throughout Year 3 & include EAC members in relevant meetings & discussions to utilize their expertise & advice with mDOT Center stakeholders.
Improve: The administration core will review and utilize the feedback given by the EAC during their Year 2 review to improve all facets of the mDOT Center research agenda and center operations.

Aim 4 - Leveraging Institutional Support for the mDOT Center
Staff: The Admin Operations team will look to retain our current staff and expand as needed and as available in Year 3 while utilizing in-kind positions and resources given by the University of Memphis.
Annual Meeting: The Admin Core will secure University spaces and facilities to host an in-person annual meeting or enterprise-level video conferencing tools and technology (if virtual) with the goal of bringing together relevant mDOT Center stakeholders for charting the Center's future research agenda.
Websites, Data, & Servers: The mDOT Center Admin team will continue to leverage, and modify as needed, the established collaborative infrastructure and computational resources developed in previous years at the University of Memphis, inclusive of hosting and storage of digital resources and data.
Data Sharing: The mDOT Center will continue to utilize Memphis IRB oversight and data sharing agreements to facilitate the accessibility of meaningful and timely data to enhance CP & SP research partnerships in Year 3.
MOODS: The mDOT Admin Operations team will continue to support the operation of this novel, innovative, and fully virtual study and will continue to support data management, participant enrollment tracking, study materials shipment, research compliance, and financial oversight of the MOODS study operations. The mDOT Software team will continue to support the study via monitoring and technical support responsiveness to the data collection and monitoring platforms.

Aim 5 - Progress Monitoring & Reporting
Reporting: In Year 3, the Admin team will compile and submit the required annual report to NIH for programmatic review.
Communication: The Admin Core staff will continue upholding the standards of responsive, thoughtful communication to continue to enhance the collaborative culture of the mDOT Center throughout Year 3.
Tracking: Utilization of current best practices for tracking goals & progress will be used by the Admin Core to create and provide a detailed, concise snapshot of mDOT Center advancement throughout Year 3 to internal members, institution officials, and external stakeholders.
Improvement: Feedback will be regularly sought from mDOT Center team members, NIH POs, affiliates, & community stakeholders.

B.2 What was accomplished under these goals?

In Year 2, the Administration core undertook the following activities to fulfill its goals.

B.2.1. Major Activities

B.2.1.1. New Flagship Software Platform for the mDOT Center

The software team works with the TR&Ds to translate their research into deployable and reusable software tools (e.g., platforms, libraries) which are then made available to the rest of the world through our common distribution channels (e.g. website, package repositories, tutorials). During this year, we developed an overarching vision for the software to be developed by the mDOT Center. We refer to it as the **mDOT-MIND (mHealth Intervention Delivery)** software platform. The MIND platform is a suite of software products that all contribute, in part, to the delivery of optimized mHealth interventions to participants in a field environment. The suite consists of (1) an app for commercial smartwatches that implement AI models for detecting health of behavioral state in real-time, (2) a cross-platform app for smartphones that anyone can install on their personal phones (both Android and iOS) which can generate real-time triggers for self-report or intervention based on the detection of events, risks, or changes in states on the smartwatch and/or the smartphone, and (3) a cloud system that can communicate with both the smartwatch and smartphone app to receive data uploads and send decisions or updated criteria for generating prompts.

To develop and test the MIND software platform, we collaborated with CP7 to conduct a fully remote user study on identifying the sources of stress that can be automatically detected by wearable devices such as a commercially available smartwatch. The study was called the MOODS (Mobile Open Observation of Daily Stressors) study.

The modules in the first version of the MIND software include a set of components that implement an IRB-compliant informed consent process for smartphones which can be reused in subsequent and additional studies with minimal changes. Additionally, wearable AI technology that measures and prompts based on participant's individual stress and non-stress episodes was built for Fossil smartwatches running WearOS. This smartwatch platform is coupled with a cross-platform, Android and iOS, smartphone app to engage with users and implements all the necessary virtual and IRB compliance requirements. This smartwatch platform contains native software modules that are necessary to provide cross-platform communications between the watch and the respective smartphone OS and are reusable for future iterations of work leveraging this platform. Both platforms integrate with a custom cloud-based API to offload data for research and study purposes.

The real-time stress detection on the Fossil smartwatch was used to generate prompts in real-time based on parameters that were initially based on population data, but were gradually personalized to be optimal for each participant. The user-specific parameters were revised at the cloud and communicated to the smartphone each time there was a bidirectional communication. These parameters were then used locally on the smartphone to decide whether a stress or non-stress episode detected on the smartwatch would be used for generating prompts. These parameters helped select which detected episodes of stress or non-stress would be selected for prompting to simulate a micro-randomized trial where user-specific parameters are used to decide when to deliver which components of a mHealth intervention.

The second major software in the mDOT-MIND platform is a standalone system designed for both software engineers and behavioral scientists as a way to include reinforcement learning into their mHealth field studies. The platform consists of a web-based tool where interventions (personalized just-in-time-adaptive interventions - pJITAIs) can be defined and configured, an API-based interface for developers to interact with published interventions, and a Python library to facilitate rapid integration with the REST API of the system.

B.2.1.2. MOODS Study for Developing and Testing mDOT-MIND Software Platform

To develop, revise, and test the mDOT-MIND software platform, we deployed it in a new user study to understand the sources of stress that can be automatically detected by wearable devices such as a commercially available smartwatch.

We pilot tested the software in fall-winter 2021 with 22 participants. The feedback elicited from these pilot participants was invaluable for testing and revising all aspects of the software. For example, multiple participants requested for a just-in-time (JIT) prompting feature to annotate stress events in real time (versus the original functionality of an end-of-day prompting to annotate all stress episodes). Starting in February, 2022 we resumed enrollment following integration and testing of study augmentations and fixing reported software bugs. To-date, all enrolled participants have opted for the JIT prompting for them to annotate their stressors soon after the stress event has occurred.

A full training and technical support infrastructure was developed by the study team to support data collection and technical support needed by participants. We developed an extensive infrastructure of study heuristics, decision trees, communications plans, and communications templates to support the data collection software platform and leverage cross-training opportunities across the study team. This planning supported continuity of study operations even in the event of disruption to study staff, and established a knowledge base for the conduct of a study of this type. We intend to share this knowledge base to support the research community: In addition to sharing necessary research compliance documents such as study protocol, consent document, and other supplemental materials, we further intend to share this compendium of study resources to help others' awareness and competencies in the design and execution of a virtual study involving wearables and wearable AI.

B.2.1.3. mHTI Support:

Due to the COVID-19 pandemic, the training program continued to be centered around a virtual consumer. The primary offering of the training core was the presentation of the all-virtual version of the annual mHealth Training Institute (mHTI). The Memphis team was instrumental in the hosting, setup, and backend administration of the virtual event.

B.2.1.4. Branding Initiative

As recommended by our Executive Advisory Committee during their review of the Center in Year 1, we launched a multifaceted digital media campaign to ensure that the mDOT Center had a unique brand and online presence with clear imaging and messaging to construct a similar, or better, brand recognition as the previously successful MD2K Center. New accounts were created on three popular social media platforms: LinkedIn, Reddit, and TikTok to make training content more accessible and to broaden the audience to include the general public. Existing Twitter and YouTube profiles were updated with logos, graphics, and wording to emphasize the mDOT Center. In addition, mDOT Center content was promoted on our various social media platforms with short blurbs to make it more attractive and digestible to our audience. Webinars were advertised with the mDOT Center logo, wording, and graphics and the title slides, social media promotions, and email announcements were redesigned to give a modern and fresh feel that is more widely appealing. The mDOT Center was highlighted as a key sponsor of the mHealth Training Institute in introductions to virtual talks and with logos on training content and promotions so that scholars were made aware of the Center's vital role in the institute. To ensure website visitors had a clear understanding of the mDOT Center and its mission, a new domain (mDOTCenter.org) was acquired for the mDOT Center. Though the mHealthHUB now includes mDOT Center branding, plans have been made for a total redesign of the layout to better meet the needs of the mHealth community and to encourage engagement with our tools and content. A final component of the rebranding effort included revising our mHealth news and correspondence. The gmail alias, group name, and welcome message as well as the team signatures, Google Docs, and outgoing communications were all revised to ensure the mDOT Center was not only reflected, but well-represented.

B.2.1.5. Meeting Facilitation

The mDOT Center Admin Team facilitated brainstorming sessions across the TR&Ds. The Center held dedicated TR&D Synergy Conference Calls in the month of April 2022. The Admin Core also hosted an in-person TR&D1 team meeting in Memphis in May 2022. The Admin Core will also host the all-hands Annual Center Meeting in-person in November 2022. Overall, the Admin Team was responsible for scheduling 138 telecons for over 70 investigators, collaborators, and staff during the project period.

B.2.1.6. New Collaborative Project (CP)

The mDOT Center added a new Collaborative Project in Year 2. Our process for vetting and admitting a new CP/SP was rigorous to ensure "fit" within the mDOT Center research mission and need within the temporally-precise mHealth intervention community. Our TR&D2 Lead, Dr. Susan Murphy, recognized a synergy with a recently awarded P50 Center that was headed by a former research colleague at the University of Michigan. The two parties agreed and plotted out the finer points of the potential push-pull relationship between the would be CP and the respective TR&Ds. A one-page proposal for the potential CP was introduced by Dr. Murphy to the mDOT Center Executive Committee. The Executive Committee, consisting of Center Leadership, reviewed the merits of the potential collaboration.

After vetting from the mDOT Center Executive Committee it was determined the P50 Center would be a good candidate for a CP spot. From here, the CP proposal was brought by the Center Director to the Executive Advisory Committee (EAC) for their review and final recommendation and upon their approval, submitted to the NIH program officer for her review and final approval.

B.2.1.7. New Executive Advisory Committee (EAC) Member

To bring fresh perspective into the EAC, the mDOT Center decided to recruit a new Executive Advisory Committee member in Year 2. It was determined that TR&D2 would benefit more from having an advisor that was in the realm of behavioral health as opposed to Machine Learning. To accommodate this, we retained our expiring TR&D2 EAC member as a consultant, and then sought out a new member to fill this spot.

The TR&D2 team first met and discussed the best qualities and expertise needed from the desired candidate. They put forth a pool of potential nominees over multiple weeks for considerations. After discussing the merits of each, the team was able to produce a short list of targets who would be ideal EAC members. The team also made a dedicated effort to balance geography, gender, and ethnicity among its candidates to further ensure a diversity of perspectives and experiences. After a few more weeks of back-and-forth discussion with some of the candidates and the TR&D2 team, a contender emerged and was formally nominated to the mDOT Center Executive Committee.

Once approved by the mDOT Center Executive Committee, the candidate was submitted to the NIH program office, before finally being introduced to the mDOT Center Team and EAC Board as its new member. This multi-week effort illustrated the process that was established by the mDOT Center Admin Core at the Center's inception and will continue to be used as members roll off and we recruit new ones.

B.2.2. Specific Objectives

Given that the inherently transdisciplinary, team-based nature of mHealth research requires scientists to cross disciplinary and institutional boundaries, administration and operation of a functional resource center in mHealth technologies requires a collaborative culture, with a team-science approach, that is geographically dispersed yet functional in a virtual setting. The mDOT Center will utilize its established and highly successful infrastructure, adaptive procedural acumen, widely visible dissemination platforms, and deeply-experienced team to develop administrative and operational policies and procedures relevant to the running of a national resource center. The Administration Core will look to not only enhance the research of the collaborative projects (CPs) and service projects (SPs), but also to streamline communication and involvement with new research groups with little or no technological expertise. The objective of the Administration Core is to provide the managerial and operational structures through which the mDOT Center will achieve its research, training, and dissemination goals. As described above, these objectives are articulated in the five specific aims.

B.2.3. Significant Results

<u>B.2.3.1. mDOT-MIND Software Suite for the MOODS Study</u>

Since last year's reporting, the MOODS study software has now been successfully used by 140 participants. We began by piloting the study software in fall-winter 2021 with 22 participants. This piloting was invaluable in the field testing and refinement of the platform, as we integrated considerable software feedback and bug reports as reported in B.2.1.2. Since the study's start, the software platform has been used by 37 participants who have completed the study. To demonstrate robustness and usability of the software platform nationwide and across a diverse set of occupational demographics, we emphasized geographic and occupational diversity. As behavioral interventions require long-term engagement, we provided weekly personalized data visualizations to see how well it can encourage participants to continue using the app for 100 days.

The study software platform has allowed us to collect and analyze 34,731 hours of wrist sensor photoplethysmograph (PPG) data that detected 88,865 events as stressed (8,103 events), non-stressed (56,943 events), or not usable for stress classification for reasons such as motion confound (23,819 events). The study software generated an average of 5 prompts per day per user, with participants responding to 80% (4 events) on average per day. This shows that participants are likely to engage in interventions for about four times per day, including moments when they a stress event may have just ended.

A manuscript reporting preliminary results from this study and the study methodology has been prepared and submitted for publication. Our study protocol has a provision for open sharing of anonymized components of this dataset following completion of the study to further support innovations in the scientific community. We expect enrollment to complete by the first-half of 2023, and further results reporting to be published in the scientific literature throughout the next year.

The MOODS software (B.2.1.1.) gained a variety of feature additions and bug fixes during the active study as previously described. The smartwatch app had a single new feature which improved the software stability and functionality when the watch's battery fully depleted and the device ran out of power. Additionally, 5 bugs were found and fixed. The most recent update to the app occurred on December 21, 2021.

The smartphone app received significantly more enhancements and bug fixes during this period. Its enhancements include a Just-In-Time annotation process, participant notification preferences, logging of system behaviors for data diagnostics and system debugging on participant devices, the ability to determine internet connectivity and show appropriate UIs when the servers are unavailable, and predictive location names and stress annotations to aid participant inputs. During this same interval, 15 bugs were identified and fixed with the most recent occurring on March 8, 2022. All enhancement and bug fixes were immediately pushed to participants through their respective app stores after internal testing was completed. This resulted in 10 unique software releases for the smartphone app during this period.

The MOODS cloud platform received an enhancement that added better annotation capabilities to support new app functionality. Additionally, it received a new feature that allowed the computation of participant stress likelihood bin thresholds necessary for the implementation of the new JIT algorithm. The platform also had 7 bugs identified and resolved in this period.

Given the software maturity (approximately 7 months without any new bugs) the mDOT-MIND platform has achieved maturity; it is now ready for additional distribution to our collaborating and service projects. We are working on recruiting additional projects that can leverage this technology to enhance their field studies.

B.2.3.2. Reinforcement Learning (RL) Software (TR&D2) (CP3)

We began the design and development of a new modular cloud-based technology stack to support reinforcement learning. This tool is a way for behavioral scientists and engineers to collaborate on designing and implementing personalized just-in-time interventions (pJITAIs) as referenced in B.2.1.1. This platform is composed of three distinct components which have been prototyped and iterated on during this period. The details of these components are described below based on what we have produced this year.

The system presents a web-based dashboard, designed in conjunction TR&D2 and CP3, where behavioral scientists are able to define their project/study. This includes things like project name and descriptions. Next, they choose the type of reinforcement algorithm for their project from a list of available one that already exist within the system. The interface then walks them through the process of setting up all the parameters (e.g., covariates, tuning parameters, decision) that are needed and/or tunable. Some of these parameters also include ineligibility criteria. This interface also provides appropriate documentation and examples throughout to better teach the behavioral scientists about the choices they are making. Once they are satisfied with the study design, they are able to publish this implementation so that the rest of the system can begin working with it. This web system has been prototyped and tested among both development teams, Memphis and Harvard. This containerization has allowed us to more quickly iterate on ideas. After initial testing, it was determined that new UIs were needed and Figma was utilized to build a new UI prototype, with input from behavioral scientists, consisting of over 40 unique screens that will need to be incorporated in year 3.

The second major component is the reinforcement learning algorithm library. This library is designed as a modular addition to the web frontend and contains the implementations of RL algorithms along with all the necessary components the pJITAI system requires to configure and run the implementations within studies. Each algorithm defines variables and parameters along with associated types and value bounds. These are organized such that the web interface can be dynamically created and modified purely based on what is defined within these algorithms.

During this year, we prototyped two algorithms, a random sampling algorithm and one based on Thompson sampling. Once these algorithms and the system are complete and tested, these will serve as templates for others wishing to add algorithms to the platform. These algorithms implement a common interface so that the rest of the platform can dynamically load and call the appropriate methods as needed. This interface consists of two methods. First, 'decision', is called whenever a request comes in that asks for a decision based on the current status of the algorithm's tuned parameters and second, `update`, which runs at a behavioral scientist specified interval and is responsible for computing/recomputing tunable parameters per user based on historical data traces. The `decision` interface is exposed through a REST protocol for interfacing with developers and other systems. The cloud platform contains a validation routing for incoming data which adds custom metadata to every decision and upload sent to the system prior to storing in its internal data store. This validation metadata is provided to each RL algorithm when they read data from the system and can individually process/handle errors as appropriate for each algorithm.

The third component is a programmatic interface to the published RL algorithms. We have built the first interface in Python, which is commonly used by developers when building backend systems to support mHealth field study applications. This interface provides an abstraction over the exposed REST interface from the pJITAI cloud. In addition to `decision`, it also implements the `upload` interface as a way to send data to the pJITAI cloud for its `update` operations. This Python interface implements some basic error checking and input/output validation for the REST protocol along with a custom object interface to make it easier to utilize. This REST interface is publicly documented on GitHub, with all the source code for this project, to make it easy for others to build custom interfaces in other languages. During this year, we published this library and 3 updates on the public python package repository (PyPi) which is available for anyone to use.

Since we are in the middle of implementing this software stack through collaborations with CP3 and TR&D2, everything we described is still a work in progress. Once completed, this tool is expected to be deployed by the researchers in CP3 as part of a pilot study without any direct involvement by mDOT software staff. As questions and bugs arise, solutions will be publicly documented and fixes pushed to the main software release. It is being designed such that any behavioral scientists with appropriate software development support could leverage the platform to significantly ease the burden of implementing reinforcement learning algorithms within their field studies.

B.2.3.3. mHTI Support

The mDOT Center admin team facilitated hosting the all-virtual mHealth Training Institute (mHTI) where mHealth training was offered to 35 scholars with 29 faculty from 20 institutions in 11 disciplines, conducted in an all-virtual environment over 13 weeks. The mDOT Center Admin Core was responsible for the entire backend and technical components of the all-virtual mHTI in Activity B.1.2.3. This entailed the creation and deployment of a team collaborative spaces (Google Drive), a comprehensive, online application management system (SmarterSelect), Lecture and Media Library (YouTube), and an informative and dynamic home page for the event participants (mHTI.md2k.org). In addition to the event management and virtual setup, the Memphis team was responsible for scheduling and communication for both scholars and faculty, collaborative environment setup (Zoom rooms, Google Drive Folders, Document Archive creation, etc.), and providing live, responsive technical support and troubleshooting support. The virtual 2022 mHTI was conducted between May 2 and July 28, 2022 (https://mhti.md2k.org/index.php/program/2022-program).

B.2.3.4. Branding Initiative

As a result of Activity B.2.1.4., the mDOT Center's online audience and engagement have grown significantly. This past year, the Center made nearly 6,000 impressions on Twitter with 33 tweets and received more than 360 engagements with our content. On LinkedIn, the Center made more than 2,600 impressions with 25 posts and received more than 40 engagements with our content. To date, the mDOT Center has an archive of over 220 videos with a combined +44,000 views via the Center's YouTube Channel. This adds up to more than 3,800 hours of asynchronous learning. Our YouTube channel has increased to more than 300 subscribers and our Twitter and Linkedin channels have a combined +400 followers. Our audience has not only grown in size, but in diversity. We have had more than 13,000 website visits to mDOTCenter.org from 138 different countries since launch.

B.2.3.5. Meeting Facilitation

The Activities of B.1.2.5. resulted in bringing our personnel together which fostered deeper collaboration and understanding. Having dedicated calls in April 2022 where each of the TR&Ds "visited" each other helped to facilitate cross-talk, familiarity of research happening, and to allow brainstorming of ideas for collaborative activities amongst the respective TR&D teams. The in-person TR&D1 Team Meeting held in Memphis, TN, coordinated and hosted by the mDOT Center Admin team, allowed for the students and investigators to come face-to-face and discuss their research agenda and network in small groups. The all-hands mDOT Center Annual Meeting traditionally is the only time of the year where all Center personnel are together in one place, at one time. It is also an open forum for the team that fosters brainstorming and is a valuable meeting where our EAC members, as well as other invited stakeholders, can give their advice and opinions regarding the mDOT Center and its future.

B.2.3.6. New Collaborative Project (CP)

Through Aim 2, with Activity B.2.1.6., we expanded the collaborative projects for the mDOT Center by one in Year 2, and will enhance the research being done in TR&D1 and TR&2. CP8 - The Center for Methodologies for Adapting & Personalizing Prevention, Treatment and Recovery Services for SUD & HIV (MAPS Center) is led by Dr. Inbal Nahum-Shani at the University of Michigan and funded by NIDA until 2026. The focus of the MAPS Center is the development, evaluation, and dissemination of novel research methodologies that are essential to optimize adaptive interventions to combat SUD/HIV. MAPS projects include developing innovative methods to optimize the integration of human-delivered services with relatively low-intensity adaptation (i.e., adaptive interventions) and digital services with high-intensity adaptation (i.e., JITAIs). MAPS aims to collaborate with TR&D1 (Marlin) by utilizing advances by TR&D1 in propagating and representing uncertainty in development of methods for adapting the timing and location of delivery of different intervention prompts. MAPS aims to collaborate with TR&D2 (Murphy) by developing methods for appropriately pooling of data from multiple users to speed up learning of both population-based decision rules as well as personalized decision rules.

B.2.3.7. New Executive Advisory Committee (EAC) Member

As part of Activity B.2.1.7. and as tied to Aim 3, when Dr. Shie Mannor's term expired we retained him as a consultant for TR&D2 and recruited Dr. David Mohr, Professor, Preventive Medicine (Behavioral Medicine), Medicinal Social Sciences, & Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine. Dr. Mohr's work lies at the intersection of behavioral science, technology, and clinical research, focusing on the design and implementation of interventions that harness digital technologies to promote mental health and wellness. He is well-versed in the use of data from smartphone and wearable sensors to identify behavioral and psychological targets that can be used for intervention. Dr. Mohr is advising the mDOT Center's TR&D2 team that develops personalized interventions and wants to work closely with behavioral health researchers. Dr. Mohr now helps to provide a voice from that community to better assess the value and utility of products coming from TR&D2 for health research.

B.2.4. Key Outcomes & Other Achievements

B.2.4.1. mDOT-MIND Software Platform for Mobile Open Observation of Daily Stressors (MOODS)

The software necessary to run the MOODS software was developed, deployed, and is in active utilization over the past year. This software consists of a cross-platform smartphone app built around Google's Flutter framework. This has allowed us to build this application for both Android and iOS. The capabilities of the app let us provide a fully functional all-virtual study infrastructure that implements the necessary IRB-approved consent mechanisms, participant enrollment and screening, and study implementation. This platform is augmented with native interface and libraries as needed to support its WearOS (Smartwatch) integration. The MOODS app is approved by both the Apple and Google app stores; however, due to study requirements the implementation is hidden within the testing environments of both where we can invite participants to join once the initial screening is complete.

A key capability for sensing is provided by a custom WearOS app running on Fossil Sport (Gen 4) smartwatches. This app utilizes undocumented APIs to provide low-level, high-frequency data access to the PPG sensors. The platform additionally records accelerometer and gyroscope sensors. This app implements our AI models that run directly on the smartwatch to enable physiological-based sensor-triggered prompting. For Android platforms, the watch utilizes a native communication mechanism; however, with iOS, we built a custom bluetooth low energy (BLE) protocol that tricks iOS into opening a communication channel to the watch in order to transmit detected episodes.

The MOODS smartphone connects to a custom REST API service that provides both data storage for episodes and the necessary routes that let the app store and recall all data that participants might see, edit, or add. This API is coupled with the high-frequency big data storage platform from MD2K, Cerebral Cortex. This API is utilized when the watches connect to a WiFi access point to upload all raw and computed data streams to the MD2K Cloud for future analysis and research.

B.4. What opportunities for training and professional development has the project provided?

All personnel working on the project learn about their own domains and collaborating domains via regular communication and collaborative research activities. In addition, they learn critical team science skills via the interdisciplinary collaborations among the investigative teams as well as by working closely with the health research team from our collaborative projects (CP). They get unique opportunities to test their ideas out by developing working software, getting regular feedback from CP investigators and their staff, and then get to test their work in real-life deployment. All personnel also learn communication skills via regular presentations and discussions. Finally, they attend relevant conferences and professional meetings to communicate and network with other members of their research community.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

A. COMPONENT COVER PAGE

Project Title: mDOT TR&D1 (Discovery) - Enabling the Discovery of Temporally-Precise Intervention Targets and Timing Triggers from mHealth Biomarkers via Uncertainty-Aware Modeling of Personalized Risk Dynamics	
Component Project Lead Information: Rehg, James M.	

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The past decade has seen tremendous advances in the ability to compute a diverse array of mobile sensor-based biomarkers in order to passively estimate health states, activities, and associated contexts (e.g. physical activity, sleep, smoking, mood, craving, stress, and geospatial context). Researchers are now engaged in the conduct of both observational and interventional field studies of increasing complexity and length that leverage mHealth sensor and biomarker technologies combined with the collection of measures of disease progression and other outcomes. As a result of the expansion of the set of available mHealth biomarkers and the push toward long-term, real-world deployment of mHealth technologies, a new set of critical gaps has emerged that were previously obscured by the focus of the field on smaller-scale proof-of-concept studies and the investigation of single biomarkers in isolation.

First, the issue of missing sensor and biomarker data in mHealth field studies has quickly become a critical problem that directly and significantly impacts many of our CPs. Issues including intermittent wireless dropouts, wearables and smartphones running out of battery power, participants forgetting to carry or wear devices, and participants exercising privacy controls can all contribute to complex patterns of missing data that significantly complicate data analysis and limit the effectiveness of sensor-informed mHealth interventions. Second, with increasing interest in the use of reinforcement learning methods to provide online adaptation of interventions for every individual, there is an urgent need for high-quality, compact and interpretable feature representations that can enable more effective learning under strict budgets on the number of interactions with patients. Finally, as in other areas that are leveraging machine learning methods to drive scientific discovery and support decision-making, mHealth needs methods that can be used to derive high-level knowledge and support causal hypothesis generation based on complex, non-linear models fit to biomarker time series data. TR&D1 will address these challenges via three specific aims:

Aim 1: Model and represent uncertainty in mHealth biomarkers to account for multifaceted uncertainty during momentary decision-making in selecting, adapting, and delivering temporally-precise mHealth interventions. This research will address the fundamental problem of missing sensor data by developing state-of-the-art deep probabilistic neural network imputation models for both raw sensor data and derived biomarkers. We will focus on developing reference imputation model architectures for widely used sensor data modalities including IMU, PPG, RIP, GPS, and key biomarkers including stress, steps, and cigarette smoking.

Aim 2: Derive uncertainty-aware composite risk scores to identify timing triggers for delivering temporally-precise interventions. This research will focus on compressing multiple biomarkers that serve as risk factors into personalized composite risk scores using novel recurrent neural network models that correctly account for biomarker uncertainty. We will develop methods for learning personalized risk models for a range of adverse events including smoking lapse, sedentary behavior, alert fatigue, and intervention disengagement. In conjunction with TR&D2, these novel risk scores will be used to drive temporally-precise adaptive interventions.

Aim 3: Model the time-varying dynamic relationships between personalized drivers of momentary risk and disease progression to identify targets of temporally-precise interventions. This research will begin to address the critical issue of providing model-based tools for identifying which potential risk factors actually impact risk in different contexts for different individuals, in order to support intervention design. To this end, we will develop methods and tools for introspecting the time-varying and contextual relationships between risk factors and risk scores learned by complex, non-linear risk scoring models developed under Aim 2.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

B.5.1. - Activity 1.1: Modeling uncertainty in irregularly sampled and incomplete multivariate time series - Our initial work on the HetVAE model was presented at the International Conference on Learning Representation in spring 2022. Our work on the BayesLDM toolbox will be presented later this fall at the IEEE/ACM Conference on Connected Health Applications, Systems and Engineering Technologies (CHASE). An arxiv preprint is available at https://arxiv.org/abs/2209.05581.

B.5.2 - Activity 1.2: Imputing Quasiperiodic Biophysical Signals - This work has been accepted for publication at NeurIPS 2022.

B.5.3 - Activity 1.3: Kernel Multimodal Continuous Attention - This work has been accepted for publication at NeurIPS 2022.

B.5.4. - Activity 2.1: mRisk - The mRisk work was published in ACM IMWUT journal and presented at the ACM UbiComp'22 conference.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In Year 3, we will undertake the following research thrusts:

Towards fulfilling Specific Aim 1, we will leverage our progress in developing novel imputation methods and mount an attack on the problem of inference in hierarchical biomarker computation graphs. This will tackle the fundamental problem of deciding where to perform imputation, given a complex biomarker computation in which some of the inputs exhibit missingness. As part of this work we will develop a unified imputation approach for irregularly-sampled data.

Towards fulfilling Specific Aim 2, we plan to continue working on developing the mRisk method with CP1 and CP5 to improve the mRisk model so that it is able to use the self-reported smoking lapses that are not supported by puffMarker detection and hence are missing the precise timing of lapse. Second, we plan to apply the mRisk model to all datasets generated in CP1 and CP5 so our health research collaborators can use it to analyze risk characteristics and pursue their publications. Third, we plan to implement the real-time version of mRisk towards the design and development of new mHealth interventions.

B.2 What was accomplished under these goals?

In Year 2, the TR&D1 undertook the following activities to fulfill its goals.

B.2.1. - Activity 1.1: *Modeling uncertainty in irregularly sampled and incomplete multivariate time series*

Our goal in Aim 1 is to model and represent uncertainty in mHealth biomarkers to account for multifaceted uncertainty during momentary decision making in selecting, adapting, and delivering temporally-precise mHealth interventions. In this period, we extended our previous deep learning approach, *Multi-Time Attention Networks,* to enable improved representation of output uncertainty. Our new approach preserves the idea of learned temporal similarity functions and adds heteroskedastic output uncertainty. The new framework is referred to as the *Heteroskedastic Variational Autoencoder*. An initial paper on this work focused on modeling real-valued multivariate data was presented at the International Conference on Learning Representation in Spring 2022 (Shukla, 2022[1]). Since then, we have been working on generalizing the space of output distributions that the model can express so it can be applied to model categorical and ordinal data from EMAs. We have also been working on the development of a specific model for imputing missing step count data in collaboration with CP3.

As a separate activity, we have also been developing a toolbox for the specification and estimation of mechanistic models in the dynamic Bayesian network family. This toolbox focuses on making it easier to specify probabilistic dynamical models for time series data and to perform Bayesian inference and imputation in the specified model given incomplete data as input. The toolbox is referred to as *BayesLDM.* A paper describing the toolbox (Tung, et. al, 2022[2]), including a modeling case study using data from CP3, was accepted for publication at the IEEE/ACM Conference on Connected Health Applications, Systems and Engineering Technologies (CHASE) and will be presented in October 2022. We have been working with members of CP3, CP4, and TR&D2 to develop offline data analysis and simulation models using this toolbox. We are also currently in discussions with members of CP4 to deploy the toolbox's Bayesian imputation methods within a live controller optimization trial in the context of an adaptive walking intervention.

[1] S.N. Shukla, B.M. Marlin. Heteroscedastic Temporal Variational Autoencoder For Irregularly Sampled Time Series. In Proceedings of the International Conference on Learning Representations. 2022.

[2] Tung, K., Torre, S.D., Mistiri, M.E., Braganca, R.B., Hekler, E.B., Pavel, M., Rivera, D.E., Klasnja, P., Spruijt-Metz, D., & Marlin, B.M. (2022). BayesLDM: A Domain-Specific Language for Probabilistic Modeling of Longitudinal Data. Accepted at IEEE/ACM international conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE) 2022. ArXiv, abs/2209.05581.

B.2.2. - Activity 1.2: *Imputing Quasiperiodic Biophysical Signals*

In support of our Aim 1 goal we have completed an investigation of a deep learning-based approach to the imputation of pulsative biophysical signals such as ECG and PPG, which are defined by a quasiperiodic morphology in terms of "beats" that are derived from the cyclic action of the cardiovascular and cardiopulmonary systems (e.g. the PQRST complex in ECG which results from the repetitive electrical activity of the heart). A broad range of wearable sensor modalities, including ECG, PPG, SCG, and so forth, exhibit such a pulsative structure, and missingness in these signals is a common challenge for mHealth researchers.

We have made progress towards this end on two fronts. First, we collected and defined the first large-scale dataset for pulsative imputation tasks, called PulseImpute, consisting of ECG and PPG waveforms from two open-source repositories, MIMIC-III Waveform and PTB-XL. In doing so, we have curated the largest clean ECG and PPG datasets, with 440,953 5-minute ECG waveforms from 32,930 patients and 151,738 5-minute-long PPG waveforms from 18,210 patients. We defined multiple imputation tasks, including real-world missingness patterns extracted from existing mHealth field studies and simulated missingness patterns derived from real mHealth missingness paradigms, such as wireless packet loss. We also defined the downstream tasks of cardiac pathophysiology classification and heartbeat detection, for the ECG and PPG modalities, which provides a means to quantify the performance of imputation algorithms in a task-specific context, on tasks that directly depended on morphological reconstruction, thereby validating the impact of imputation on biomarker computations.

Second, we developed a state-of-the-art attention-based deep learning transformer architecture that can learn to leverage the quasi-periodic signal structure to perform accurate imputation in the face of substantial amounts of missingness, such as the absence of multiple beats. We have validated that this novel transformer-based imputation method outperforms existing standard imputation baselines. These findings are reported in a paper (Xu, et. al., 2022[3]) that was accepted for publication at NeurIPS 2022.

[3] M. A. Xu, A. Moreno, S. Nagesh, V. B. Aydemir, D. W. Wetter, S. Kumar, and J. M. Rehg. PulseImpute: A Novel Benchmark Task for Pulsative Physiological Signal Imputation. Proceedings 36th Conference on Neural Information Processing Systems (NeurIPS), Track on Datasets and Benchmarks, 2022. Accepted for publication. NIHMS1839168.

B.2.3 - Activity 1.3: *Kernel Multimodal Continuous Attention*

One technical challenge in modeling missingness in biomarker streams is the need to develop flexible attention mechanisms that can learn to focus on the relevant aspects of an input signal. We have completed the development of a novel continuous-time attention model which is capable of learning *multimodal* densities, meaning that the attention density can be focused on multiple signal regions simultaneously. Classical solutions like Gaussian mixtures have dense support, with the result that all regions of a signal have some probability mass, making it difficult to focus the attention on key regions and ignore irrelevant ones. Our work introduces kernel deformed exponential families, a sparse class of multimodal attention densities.

B.2.4. - Activity 2.1: *mRisk: Sensing the Imminent Risk of Impulsive Behavior Using Mobile Sensors*

Our goal in Aim 2 is to derive uncertainty-aware composite risk scores to identify timing triggers for delivering temporally-precise interventions. We reported in Year 1 that had been working on developing machine learning models to passively and continuously detect dynamically varying composite risk score for the impulsive adverse behavior smoking lapse that combines factors internal to an individual (e.g., stress, craving, and self-efficacy) and those external to them such as exposure to risky environments (e.g., geo-exposures to smoking spots or tobacco point of sale). Estimation of the continuous risk state may be critical for delivering temporally-precise interventions and treatment adaptations in cessation programs. We worked with CP1 (Novel Use of mHealth Data to Identify States of Vulnerability and Receptivity to JITAIs) and CP5 (Affective Science and Smoking Cessation: Real-time Real-world Assessment) for its incorporation into the study to fully develop a first version of this model called *mRisk*. We addressed several technical challenges. First, continuous sensor data collected from wearables and smartphones to capture risk factors of adverse behaviors in the natural environment are usually noisy and incomplete. Second, for adverse behavioral events such as a smoking lapse, capturing the precise timing of each smoking lapse may not be feasible, as sensors may not be worn at the time of a lapse or the lapse events may not be accurately detected due to the imperfection of machine learning models that are used to detect smoking events via hand-to-mouth gestures. Therefore, only a few positive events (i.e., smoking lapse in a cessation attempt) are available. Third, confirmed negative labels can be assigned to a block of sensor data corresponding to a prediction window only if the entire time period is confirmed to have no high-risk moment. As not all high-risk moments may result in a lapse, labeling a block of sensor data to the negative class is difficult for such events. We addressed each of these challenges in developing the mRisk model. Specifically, we encoded sensor data as events to handle noise and missingness, modeled the historical influence of recent psychological, behavioral, and environmental events via deep learning model and addressed the issue of lack of negative labels and only a small subset of positive labels by using a positive-unlabeled framework with a novel loss function. We analyzed 1,012 days of sensor data collected by 92 newly abstinent smokers to train and evaluate the mRisk model.

B.2.5. - Activity 2.2: *Prediction of EMA Nonresponse Using Transformers*

The collection of self-reported data from participants via EMA is a key tool that is used in mHealth studies to identify the timing and occurrence of outcomes such as relapse to smoking and to obtain information about mood and behavioral states such as craving which are difficult to measure from passive sensing. A major challenge in EMA data collection is non-response, when participants fail to provide EMA items in response to a prompt. We have developed a transformer-based deep learning architecture for predicting nonresponse given a history of past EMA responses in conjunction with demographic and contextual data. Prior work on non-response prediction has only used classical machine learning methods. This work is the first to explore the utility of transformers on EMA data in general and for non-response prediction specifically. Our novel approach outperforms classical machine learning methods on average by 0.1 AUROC with transformers having a clear advantage at modeling longer sequences. We designed a self-supervised task of EMA imputation that aims to capture the structure across different EMA items. This task proves to be an effective pre-training task that improves non-response prediction performance.

A challenge specific to EMA data is that the items differ across studies based on the research aim. This results in EMA data from different studies lying in different input-spaces, a phenomenon we refer to as covariate-space shift. Covariate-space shift is a challenge to data pooling to utilize data from multiple studies, transferring a model trained on one EMA study to another, and using domain adaptation methods to develop models that generalize well across studies. We design a valence representation to capture positive and negative emotions from EMA responses irrespective of the fine-grained items. The valence representation is a common representation across studies while yielding a comparable non-response prediction performance as dataset-specific representations. This enables data pooling and domain adaptation which improve non-response prediction and generalization performance respectively.

B.2.6. - *Summary of Push-Pull Activities with CPs*

CP1 (Nahum-Shani) & CP5 (Lam/Wetter): The CP1 and CP5 teams are specifically interested in risk prediction problems based on mobile sensor and EMA data to support the development of novel interventions for smoking cessation. TR&D1 investigator Kumar collaborated with CP1 and CP5 on the challenges of smoking lapse prediction which directly influenced the mRisk (Ullah, et. al, 2022[4]) work under Aim 2 Activity 2.1 and led to a joint publication. TR&D1 investigator Rehg also worked closely with the CPs on the nonresponse prediction problem in EMA data which led to Activity 2.2. Additional work on biophysical signal imputation and continuous-time attention models in Activities 1.2 and 1.3 is a direct result of a dialog with CP1 and CP5, based on concerns about dealing with missing sensor data when building models for risk prediction. These works will be further integrated with CP activities in Year 3.

[4] Md Azim Ullah, Soujanya Chatterjee, Christopher P. Fagundes, Cho Lam, Inbal Nahum-Shani, James M. Rehg, David W. Wetter, and Santosh Kumar. 2022. mRisk: Continuous Risk Estimation for Smoking Lapse from Noisy Sensor Data with Incomplete and Positive-Only Labels. Proc. ACM Interact. Mob. Wearable Ubiquitous Technol. 6, 3, Article 143 (September 2022), 29 pages.

CP3 (Klasnja): We are working closely with the CP3 team to build test cases for the BayesLDM toolbox as well as to learn missing data imputation models for FitBit step data using the HetVAE model. CP3 is providing data and model specifications. TR&D1 is providing modeling tools and inference results to further CP3's data analysis goals.

CP4 (Rivera): We are working with CP4 to deploy a BayesLDM model in a live controller optimization trial. CP4 is investigating the integration of BayesLDM into their computing platform and is developing BayesLDM models for their problem domain. CP4 is providing example models to evaluate the computational scalability of BayesLDM as well as specifications for additional toolbox functionality. TR&D1 has made the BayesLDM toolbox available for use by members of CP4 and is providing support and code updates to implement requested functionality.

CP8 (Nahum-Shani): We are working with CP8 to explore an improved formulation of imputation which leverages feature learning and delivers improved imputation accuracy. We are doing this in the context of EMA data using a novel transformer architecture which is able to deliver improved imputation accuracy. CP8 is providing guidance on identifying baseline imputation methods and we are collaborating to define best practices for selecting imputation methods for offline data analysis and validating those choices.

B.2.2. Specific Objectives

TR&D1 will develop, evaluate and disseminate methods to analyze population-scale multi-modal time series of mHealth biomarkers to enable research on identifying the momentary risk factors and risk dynamics that drive adverse health outcomes while accounting for the uncertainty and missingness inherent in these data sources. Based on the research conducted under the above aims, TR&D1 will produce toolboxes and cloud-based data analysis tools for missing data modeling and imputation, uncertainty-aware personalized risk scoring, and introspection of complex risk scoring models. These tools will address critical gaps in the current mHealth technology landscape and will provide transformative capabilities for both advancing the understanding of health and behavior and for supporting the design of temporally-precise, sensor-based mHealth interventions.

B.2.3. Significant Results

B.2.3.1. - *Modeling uncertainty in irregularly sampled and incomplete multivariate time series*

Our initial work on Heteroskedastic Variational Autoencoders (HetVAEs) was shown to provide performance improvements over our prior multi-time attention network (mTAN) approach. This work was presented at the International Conference on Learning Representation in spring 2022. Our work on the BayesLDM toolbox will be presented later this fall at the IEEE/ACM Conference on Connected Health Applications, Systems and Engineering Technologies (CHASE). BayesLDM provides a domain-specific model language interface to the toolbox that significantly simplifies the expression of probabilistic dynamical systems models as well as inference programs for these models when the available data contain missing data, which is almost always the case in mHealth modeling tasks.

B.2.3.2. - *Imputing Quasiperiodic Biophysical Signals*

The novel PulseImpute dataset is the first large-scale dataset containing complex imputation tasks for pulsative biophysical signals. State-of-the-art imputation methods from the time series literature are shown to exhibit poor performance on PulseImpute, demonstrating that the missingness patterns emerging in mHealth applications represent a unique and important class of imputation problems. By releasing this dataset and a new state-of-the-art baseline algorithm, we hope to spur the ML community to begin addressing these challenging problems. This work was accepted for publication (Moreno, 2022[5]) at NeurIPS 2022.

[5] A. Moreno, Z. Wu, S. Nagesh, W. Dempsey, and J. M. Rehg. Kernel Multimodal Continuous Attention. Proceedings 36th Conference on Neural Information Processing Systems (NeurIPS), 2022. Accepted for publication

B.2.3.3 - *Kernel Multimodal Continuous Attention*

We theoretically analysed the normalization, approximation, and numerical integration properties of this density class. We applied these densities in analyzing real-world time series data and showed that the densities often capture the most salient aspects of an input signal, and outperform baseline density models on a diverse set of tasks. These findings are reported in a paper that was accepted for publication at NeurIPS 2022.

B.2.3.4. - *mRisk: Sensing the Imminent Risk of Impulsive Behavior Using Mobile Sensors*

The mRisk method has been developed and evaluated on a dataset of 92 participants (newly abstinent smokers) obtained from CP1 and CP5. We find that 85% of lapses can be intervened upon with about 5.5 interventions per day. By analyzing the risk dynamics around lapse moments, we discover that risk usually peaks 44 minutes prior to a lapse. By using SHAP to explain the influence of different contexts on lapse risk we find that a recent visit to a smoking spot has the highest influence on risk, followed by stress. This work was accepted in ACM IMWUT journal and presented at the ACM UbiComp'22 conference.

B.2.4. Key Outcomes & Other Achievements

B.2.4.1. - The HetVAE codebase was released at https://github.com/reml-lab/hetvae

B.2.4.2. - The BayesLDM toolbox and user guide were released at https://github.com/reml-lab/BayesLDM

TR&D1 - Discovery	Books	Papers	Abstracts
Number Published	0	2	0
Number in Press	0	3	0
Number in Submission/Review	0	1	0

B.4. What opportunities for training and professional development has the project provided?

At UMass Amherst, two students received training in the development of machine learning methods for incomplete and irregularly sampled data. Both students had the opportunity to participate in telecons with CP3 and CP4 investigators as well as on mDOT Center telecons. One of the two students is also participating in TR&D2 & is jointly mentored by Co-I's Marlin and Murphy as well as CP3 PI Klasnja. At Georgia Tech, four students received training in the development of machine learning methods for analyzing biophysical and EMA signals and developing attention mechanisms. These students participated in telecons with investigators from CP1, CP5, and CP8 as well as with the mDOT Center telecons. PhD student Alex Moreno successfully defended his dissertation and graduated in 2022. At Memphis, one student participated in TR&D1 telecons and directly worked with Georgia Tech investigator and those from CP1 and CP5 to receive multidisciplinary training in developing novel machine learning model for mRisk.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?
Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?
Not Applicable
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?
NOTHING TO REPORT
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

A. COMPONENT COVER PAGE

Project Title: mDOT TR&D2 (Optimization): Dynamic Optimization of Continuously Adapting mHealth Interventions via Prudent, Statistically Efficient, and Coherent Reinforcement Learning
Component Project Lead Information: MURPHY, SUSAN A

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Mobile health (mHealth) interventions have typically used hand-crafted decision rules that map from biomarkers of an individual's state to the selection of interventions. Recently, reinforcement learning (RL) has emerged as a promising approach for online optimization of decision rules. Continuous, passive detection of the individual's state using mHealth biomarkers enables dynamic deployment of decision rules at the right moment, i.e., as and when events of interest are detected from sensors. RL-based optimization methods that leverage this new capability created by sensor-based biomarkers, can enable the development and optimization of temporally-precise mHealth interventions, overcoming the significant limitations of static, one-size-fits-all decision rules. Such next-generation interventions have the potential to lead to greater treatment efficacy and improved long-term engagement.

However, there exist several critical challenges to the realization of effective, real-world RL-based interventions including the need to learn efficiently based on limited interactions with an individual while accounting for longer-term effects of intervention decisions, (i.e., to avoid habituation and ensure continued engagement), and accommodating multiple intervention components operating at different time scales and targeting different outcomes. As a result, the use of RL in mHealth interventions has mostly been limited to very few studies using basic RL methods.

To address these critical challenges, TR&D2 will build on more precise biomarkers of context, including TR&D1 risk and engagement scores, to develop, evaluate, and disseminate robust and data-efficient RL methods and tools. These methods will continually personalize the selection, adaptation and delivery timing decision rules for core intervention components so as to maximize long-term therapeutic efficacy and engagement for every individual. TR&D2 will address these challenges via the following three specific aims:

Aim 1: Accounting for delayed treatment effects via prudent learning of decision rules. Generalize current myopic Bandit RL methods to enable learning non-myopic decision rules that account for delayed intervention effects. A particular focus is delayed effects due to intervention burden.

Aim 2: Efficient personalization via optimizing data sharing across users. Develop RL methods that personalize decision rules for every individual by optimally leveraging data across a population or cohort to accelerate learning. We will further develop RL methods to facilitate the analysis of the resulting data, taking into account the additional correlation structure that results from partial between-person sharing of data during learning.

Aim 3: Coherent learning of decision rules across intervention components operating at different time scales and with different objectives. Increasingly, mobile interventions include multiple components targeting different outcomes (e.g., stress, inactivity) and time scales (e.g., within day, daily). We will develop approaches to use distal health outcomes to guide learning for these multiple components, so as to minimize negative interactions.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : TR&D2 B.2. ACCOMPLISHMENTS.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The primary mechanisms of dissemination have been technical papers and seminar talks. Please see the publications and presentations (Section C - Products in the Overall). Further, we mentor a number of young health scientists who are running MRTs. These include health scientists at Harvard Medical School, Children’s Hospital of Philadelphia, University of Michigan Medical School, Children’s National Hospital, and Johns Hopkins University.
Also, we collaborate on review/expository papers so as to improve dissemination. These include papers in Psychiatry[1], and in Biostatistics[2].

[1] Coppersmith, D.L., Dempsey, W., Kleiman, E.M., Bentley, K.H., Murphy, S.A., & Nock, M.K. (2022) Just-in-Time Adaptive Interventions for Suicide Prevention: Promise, Challenges, and Future Directions, Psychiatry.

[2] Qian, T., Cohn, E. and S.A. Murphy,(202?) Statistical Designs for Developing Personalized Mobile Treatment Interventions, Book chapter to appear in Digital Therapeutics: Scientific, Statistical, Clinical, and Regulatory Development Aspects , edited by O. Sverdlov and J. van Dam,, Chapman & Hall/CRC.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In Year 3, we will undertake the following research thrusts:

In Year 3, CP2 and CP8 will run clinical trials deploying our RL algorithms. These RL algorithms will pool data (Aim 2) across individuals in order to personalize. We will finalize and provide a protocol for the algorithms. Further, both algorithms will be using approaches developed under Aim 1 to allow the RL algorithm to account for delayed effects. These trials will allow for first real-life evaluations of the RL algorithmic research conducted under Aims 1,2.

We will continue the work (in collaboration with CP3) of the toolbox. CP3 will conduct a user study that will then allow us to refine the toolbox. This toolbox will allow us to more effectively disseminate our RL algorithm developments. We aim to have a first version for use by health scientists and in particular our SPs this year.

We aim to start making greater progress on Aim 3, particularly with regards to the use of intermediate outcomes of treatments by the RL algorithm. This work will also involve generalizing RL algorithms to be able to accommodate both delayed observations of state and reward.

B.2 What was accomplished under these goals?

In Year 2, the TR&D2 undertook a variety of activities (as described below) to fulfill its goals.

B.2. Major Activities (include push-pull activities with CPs)

B.2.1. - Activity 1: *Reinforcement Learning (RL) Algorithms*

Development of an RL algorithm (Aims 1,2) and inference from an MRT employing an RL algorithm (Aim 2): This research was motivated by and spurred on by our collaborations with CP2 and CP8. In particular, CP2 will conduct a MRT (mHealth intervention to improve oral health) using our developed RL algorithm (Trella et al. 2022[1], Trella et al.[2], in review) in early 2023. In Trella et al. 2022[1] we generalized best practice principles from machine learning to the field of reinforcement learning and provided pre-implementation guidelines (Aim 2). In Trella et al.[2], (in review) we developed an approach to designing the reward function so that the RL algorithm would learn faster (Aim 1). This paper received positive reviews. The graduate students in our lab have been working with CP2's software engineers and app developers to ensure that the RL algorithm is stably implemented (this work will continue into the next year).

In both the oral health trial (CP2; early 2023) and a cannabis reduction trial (CP8; late 2023) we are developing and will deploy an RL algorithm that autonomously pools data across individuals in order to personalize the mHealth intervention to each individual during the study. This pooling of data by the RL algorithm produces dependence between individuals in the studies (called "adaptive sampling"). This is highly problematic as these are/will be registered clinical trials and thus primary data analysis methods must be justified and pre-specified. It was incumbent on our team to develop the mathematical theory and associated statistical methodology/measures of confidence that allow our collaborators to pre-specify the primary data analysis methods before they conduct these clinical trials. The mathematical theory is non-trivial. We are thrilled to report that we have successfully developed the theory (Zhang et al, 2022[3])! This work is under revision for a theoretical publication. An RL algorithm that autonomously pools data to learn faster can now be used in these two trials.

[1] A. Trella, K. Zhang, I. Nahum-Shani, V. Shetty, F. Doshi-Velez, S. Murphy. Designing Reinforcement Learning Algorithms for Digital Interventions: Pre-implementation Guidelines. Algorithms 2022, 15(8), 255.

[2] A. Trella, K. Zhang, I. Nahum-Shani, V. Shetty, F. Doshi-Velez, and S. Murphy. Reward Design For An Online Reinforcement Learning Algorithm Supporting Oral Self-Care.

[3] K. Zhang, L. Janson, S. Murphy. Statistical Inference After Adaptive Sampling in Non-Markovian Environments.

B.2.2. - Activity 2: *RL Toolbox (pJITAI)*

Designing an mDOT Center toolbox called pJITAI that health scientists can use to design their RL algorithm for use in conducting their mHealth study (All Aims; Dissemination): This work is in collaboration with CP3 (physical activity). Translating very technical ideas (methods for constructing RL algorithms) into language and guidelines that can be used by behavioral health scientists turns out to be very challenging. A postdoc in our lab is working with a CP3 graduate student and software engineers in Memphis; they have constructed the wireframes for use in the user studies (here the "user" is the behavioral scientist). We have revised these wireframes in response to work with two users (both behavioral health scientists who are conducting MRTs). We also have a draft of the associated tutorial.

B.2.3. - Activity 3: *RL and Context Inference*

Generalize current myopic Bandit RL methods to enable learning non-myopic decision rules that account for delayed intervention effects (Aim 1): Working with TR&D1 and CP3, we are investigating the application of deep learning-based RL methods to RL simulation environments based on key properties of contextualized messaging interventions. This work focuses on evaluating the effect of missing and incomplete data on the ability of deep learning-based RL methods to learn policies in domains with delayed treatment effects. It is particularly concerned with the problem of accounting for uncertainty in context inferences that are used as part of the RL state.

B.2.4. - *Summary of Push Pull Activities with CPs*

CP1 (Nahum-Shani): We collaborated on four papers with CP1. Two of the papers (Nahum-Shani et al, 2023[4],2022[5]) concern the thorny issue of engagement in mHealth. This critical "domain science" work will inform our future work on Aim 3. The third paper[6], a collaboration between CP1, CP3, and TR&D2, is an in-depth introduction and tutorial on MRT experimental design and data analysis for quantitative psychologists (an important dissemination target). The fourth[7] paper reports on the data analysis of an MRT aimed at increasing engagement in mHealth by young adults who exhibit problematic use of drugs (The data analysis methods were developed, in prior years, by our lab). And the last paper[8] reports on the design of a smoking cessation MRT that is in the field.

[4] Nahum-Shani, I., Wetter, D. and Murphy, S.A. (2023) Adapting just-in-time interventions to vulnerability and receptivity: Conceptual and methodological considerations, Book chapter to appear in Digital Therapeutics for Mental Health and Addiction: State of the Science and Vision for the Future , edited by Nick Jacobson, Tobias Kowatsch, and Lisa Marsch, Elsevier.

[5] Nahum-Shani I, Shaw SD, Carpenter SM, Murphy SA, Yoon C. Engagement in digital interventions. Am Psychol. 2022 Mar 17.

[6] Qian T, Walton AE, Collins LM, Klasnja P, Lanza ST, Nahum-Shani I, Rabbi M, Russell MA, Walton MA, Yoo H, Murphy SA. The microrandomized trial for developing digital interventions: Experimental design and data analysis considerations. Psychol Methods. 2022 Jan 13.

[7] Nahum-Shani I, Rabbi M, Yap J, Philyaw-Kotov ML, Klasnja P, Bonar EE, Cunningham RM, Murphy SA, Walton MA. Translating strategies for promoting engagement in mobile health: A proof-of-concept microrandomized trial. Health Psychol. 2021 Dec;40(12):974-987.

[8] Nahum-Shani I, Potter LN, Lam CY, Yap J, Moreno A, Stoffel R, Wu Z, Wan N, Dempsey W, Kumar S, Ertin E, Murphy SA, Rehg JM, Wetter DW. The mobile assistance for regulating smoking (MARS) micro-randomized trial design protocol. Contemp Clin Trials. 2021 Nov;110:106513.

CP2 (**Shetty**): The collaborations with CP2 have been extensive and are reported under B2: Activity 1. Graduate students in our lab worked with a postdoc in CP2's lab on how to use the message content developed by CP2 with our RL algorithm.

CP3 (Klasnja): Collaborations with CP3 have also been extensive and are reported under B2: Activity 2 and Activity 3. Further, we submitted a joint grant application to NHLBI--this application proposes to build on ideas under Aim 1 of this grant to design an RL algorithm that uses causal diagrams to build a reward function that takes into account the delayed effects of the treatments on distal outcomes. We also collaborated on three papers. The first two papers concern off-policy RL and span all three aims (Liao et al[9], to appear; Bertsimas et al[10], to appear). The third paper, a collaboration between CP1, CP3, and TR&D2, is an in-depth introduction and tutorial on MRT experimental design and data analysis for quantitative psychologists (an important dissemination target).

[9] P. Liao, Z. Qi, R. Wan, P. Klasnja, S. Murphy Batch Policy Learning in Average Reward Markov Decision Processes. To appear in the Annals of Statistics.

[10] Bertsimas D., Klasnja, P., Murphy, S., & L. Na (2022) Data-driven Interpretable Policy Construction for Personalized Mobile Health (to appear as a regular full paper in 2022 IEEE International Conference on Digital Health).

CP8 (Nahum-Shani): CP8 is a new collaborative project. We are currently engaged in a push-pull collaboration with CP8 with regards to the development of a pooling RL algorithm (Aim 2) to be deployed in 2023 in a small mHealth trial for young adults who are exhibiting problematic use of cannabis (see Activity 1 under B2). One of the graduate students in our lab is working with CP8's software engineer. This work by our graduate student and CP8's software engineer is being informed by our lab's work with CP2's software engineering team.

B.2.2. Specific Objectives

TR&D2 will address three key limitations of current online reinforcement learning (RL) when applied to personalize mobile interventions to individuals. Two of these limitations are related to the need to increase efficacy and reduce negative delayed intervention burden effects leading to disengagement. The third looks to future needs involving the personalization of multiple intervention components each operating at a different time scale. In particular, the mDOT Center will accommodate the ever-present mobile health challenge of user disengagement by developing a continuum of approaches between RL algorithms that ignore delayed intervention effects and RL algorithms that attempt to capture noisy delayed intervention effects over a more distant future. Second, the mDOT Center will increase the rate at which personalization occurs via optimally leveraging data across time and across users to more quickly personalize the interventions to each user. Third, the mDOT Center will develop the first RL approaches to coherently personalize multiple intervention components holistically. In addition, to enhance impact and dissemination, the methods will be developed in close collaboration with designated collaborative projects (CPs) with an emphasis on model interpretability. TR&D2 will create a toolkit for online intervention optimization that will include cloud-based modules for personalizing adaptation rules as well as smartphone modules implementing real-time intervention selection. TR&D2 will also produce a reference tutorial for use of the online intervention optimization toolkit. Both tools will be implemented within the mDOT Center software framework and will enable a broad segment of the mHealth research community to continuously optimize mHealth intervention rules, so as to achieve optimal efficacy and engagement for individuals despite dynamic variations in the physical, behavioral, social, and environmental states.

B.2.3. Significant Results (including major findings, developments, or conclusions both positive and negative)

Our most significant breakthrough was the successful development of the mathematical theory that provides measures of confidence when the RL algorithm pools data across individuals in order to personalize during a clinical trial. We are now able to further develop and deploy this type of algorithm in clinical trials. This is a major step forward for the use of personalization algorithms in mHealth clinical trials.

TR&D2 - Optimization	Books	Papers	Abstracts
Number Published	0	7	0
Number in Press	2 chapters	2	0
Number in Submission/Review	0	2	0

B.4. What opportunities for training and professional development has the project provided?

Murphy runs weekly brainstorming sessions through her lab at Harvard. At these brainstorming sessions, a postdoc or graduate student in our lab presents a research idea and everyone in the lab brainstorms about how to help that person. Brainstorming sessions are also run with health scientists (in early January 2022 we conducted a brainstorming session with Australian health scientists who are to conduct an MRT in mobile health for adolescents with mental health problems). An important aspect of the brainstorming is that attendees learn to present their ideas concisely and to communicate across disciplinary boundaries. Attendees include computer scientists, electrical engineers, operations research scientists, statisticians, and health scientists. Further, Murphy participated (presented and mentored a team) in the mHealth Training Institute 2022 (see mHealth Training Institute - 2022 Program).

Marlin and Murphy are also jointly mentoring one student at UMass Amherst who is working on Activity 3 listed under section B.2. They meet together with the student biweekly along with CP3 PI, Klasnja. This student also attends separate weekly meetings with the complete CP3 project team including Marlin and Klasnja. These opportunities are providing the student with training in RL applied to behavioral science as well as diverse exposure to behavioral theory and modeling.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

The mDOT Center toolbox is expected to lead to new practices by health scientists--this toolbox will enable them to design their own RL algorithm. Early indications from health scientists are very positive.

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

A. COMPONENT COVER PAGE

Project Title: mDOT TR&D3 (Translation): Translation of Temporally Precise mHealth via Efficient and Embeddable Privacy-aware Biomarker Implementations	
Component Project Lead Information: Ertin, Emre	

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Vigorous research activity in mHealth has resulted in an ever-growing list of physiological and behavioral markers. However, translation of these biomarkers into real-time intervention lagged behind the observational research studies that led to their development due to computation, storage, and communication bottlenecks faced by wearables and smartphone platforms. Further, the next generation of wearables is emerging with the ability to sample data from multiple sensors at rates several orders of magnitude higher than current-generation devices, exacerbating the computational and communication bottleneck. They can image structure, motion, and function, to provide visibility into physiology previously possible only in clinics.

Traditionally, such imaging sensors use post-processing algorithms for feature identification, co-registration, alignment, and enhancement. However, high-frequency high-volume imaging data from wearables cannot be transported to cloud computing for post-processing. Finally, researchers have shown that the high-dimensionality sensor data needed to compute biomarkers presents immense privacy risks. Advances in machine learning are leading to an ever-growing list of surprising inferences about user identity and activities that can be made from seemingly innocuous sensors, particularly when data are captured over long durations. Simplistic methods such as stripping personally identifiable information and addition of noise that focus on anonymizing the data have been ineffective for mHealth, both from privacy and utility perspectives, particularly with the availability of vast amounts of side information (e.g. metadata), computational power, and advanced algorithms.

To address these growing challenges, we propose a hierarchical computing framework that reduces the data into minimal modular abstractions called Micromarkers computed at the edge devices. Micromarkers can be used directly as features in new biomarker inferences or can be adapted to support legacy algorithms. TR&D3 will develop hardware, software, and computational techniques to implement privacy-aware, efficient, and embedded intelligence support into wearables. They will enable continuous, high-throughput, low latency biomarker captures across wearable, mobile, and cloud platforms to support large-scale and long-term research studies and eventual real-life rollout. TR&D3 will pursue the following specific aims:

Aim 1: Develop modular and reusable micromarker abstractions to enable resource-efficient concurrent computation of a growing collection of biomarkers: Develop hierarchical computing methods and tools to support scalable, low-latency, power-efficient computation of current and emerging biomarkers. Modular Micromarker abstractions will be used to compress information relevant to biomarker computations at the edge devices while stripping nuisance variables such as hardware biases/drifts and background levels that are not pertinent to inference.

Aim 2: Create signal processing architectures combining Compressive Sensing and Machine Learning algorithms to support biomarker computations on resource-constrained high data rate sensor arrays: Develop and disseminate configurable sensor hardware prototypes and data-driven methods for resource-efficient denoising, signal reconstruction, and deblurring to enable real-time computation of biomarkers from the next generation of sensor modalities employing sensor arrays.

Aim 3: Enable optimization of privacy-utility tradeoffs in biomarker computations via cross-layer mechanism design: Create computational mechanisms and a general biomarker privacy framework to enable participant control over the privacy-utility tradeoffs during study design, data collection, and sharing of collected mHealth data for third-party research when data cross trust domains.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File Uploaded : B.4. TR&D3 TRAINING.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The primary mechanisms of dissemination have been technical papers, seminars, and other invited talks related to TR&D3 research. In particular, Srivastava gave invited keynote talks at IEEE CogMI 2021, NSysS 2021, and ACM MobiSys 2022; and, seminar talks at Amazon Science and SRC eWorkshop. Additionally, Srivastava co-organized the Trustworthy AI Day at ACM KDD 2022, the top data science conference. Kumar was a panel speaker at the event, which also had additional invited speakers from industry, government, and academia. A significant part of the event was focused on exploring issues of trust and privacy in the context of mobile health systems. Srivastava's group also engaged in the tinyML community which is the leading organization for AI/ML on resource-constrained platforms. Lastly, Srivastava contributed to the Expert Ad HoC Committee for Global Electronics Council's "Wearables: Product Data Privacy and Information Security Criteria" standard.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

In Year 3, we will undertake the following research thrusts:

For the micromaker framework, we aim to improve privacy-preserving features by including explicitly a discriminator/critic trained to penalize information that will aid in re-identify subjects based on sensor data driving inspiration from the training setup of generative adversarial networks. We will also explore the tradeoff between the compression ratio and tabulate task-specific performance as a function of the compression ratio.

For the BioRF imaging thrust, we will continue to explore computationally efficient methods for contrast imaging using deep learning-based methods. We will use empirical data from human tissue phantoms to learn and encode the spatial structure of the tissue profile data act as a regularizer in the inverse imaging. We will also study methods to simultaneously estimate the tissue profiles (permittivity, conductivity) and electromagnetic variables of interest such as electric field strength rather than methods that target tissue profile only. Joint estimation of EM parameters has the advantage of regularizing the solution further using physics principles.

For our RF and Motionsense platform, we will continue to develop firmware that will support direct TensorFlow module access to the sensor data streams. This will enable researchers outside TRD3 to experiment with their algorithms directly at these edge devices with full access to data with no latency or bandwidth restrictions. We will also experiment with flexible patch antenna designs that will allow researchers to tailor the bandwidth, center frequency, and size of the antennas to explore density and penetration depth tradeoffs in their particular applications of interest.

We will continue the two activities that we initiated this year and which are still ongoing: understanding reidentification risks from sharing processed sensor data, and understanding factors that affect users' perception of privacy with wearable and ambient sensor devices monitoring biomarkers and delivering interventions.

We will build upon our work on platform-aware neural architecture search to consider architecture search for neuro-symbolic models (that combine neural models with first-principles/physics) on ultra-resource constrained platforms.

Going beyond privacy-aware sharing of data for biomarker computation, we will examine privacy and trust issues in the full sensing-biomarker-intervention-delivery loop across edge-cloud. Specifically, we will target (i) Risks from predictions different from past/present, which can't be defended with counter-evidence, difficult to explain; (ii) Ensuring delivery of intervention to the valid user, which requires continually authenticating the user; (iii) Delivering intervention in a privacy-sensitive manner, which would require adapting delivery to the device (wearable, mobile, ambient), modality (visual, acoustic, haptic), and context (e.g., presence of others, location, physical state, etc.); and (iv) Challenges arising from interventions that use explore-exploit paradigms (e.g., deep reinforcement learning) that depend on “probes”, such as leak of information about personal preferences, behaviors, and contexts.

B.2 What was accomplished under these goals?

In Year 2, the TR&D3 undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. Major Activities (include push-pull activities with CPs)

B.2.1.1. - Activity 1.1 (Aim 1): *Learning Task Specific Autoencoders for creating micromarkers of PPG data*

We continued our work in learning autoencoder structures to extract heart rate and heart rate variability information from multichannel sensor data, while stripping information that is sensor or subject related information not relevant to the inference tasks at hand. This activity is in support of our goal in Aim 1 to develop hierarchical computing methods to support the scalable, low-latency, power-efficient computation of biomarker computations. We use a multichannel autoencoder structure paired with a tachogram estimation based on convolutional neural networks as an end-to-end trainable algorithm using a task-specific error metric that penalizes deviations from the actual tachogram signal derived from an ECG sensor during training. Then we use the latent codes learned in the autoencoder framework as the micromarker representations of the heart rate signal that are tailored for tachogram estimation. This year we have enriched the meta-task to include performance metrics that penalizes both frequency and time domain features. This allows the pairing of our task specific autoencoder with legacy algorithms that rely on the time and frequency domain features of the tachogram signal.

B.2.1.2. - Activity 1.2 (Aim 2): *RF Imaging at Edge Devices*

RF imaging is a new sensor modality that uses electromagnetic waves scattered from internal tissues to understand internal structure with applications to heart motion/contractility monitoring, and lung water estimation. The aim is to create a contrast image that provides information about the different permittivities of the tissues under interrogation. Traditional imaging methods, such as contrast inversion, attempt to invert Maxwell's equations through computationally intensive iterative methods. These imaging modalities are not suitable for implementation on edge devices. We follow a computationally attractive deep learning method for contrast image construction that builds on our micromarker framework. Using task specific autoencoders, we first learn a latent space representation for contrast images obtained from ground truth data from simulations and body phantom measurements. Next, we train a deep neural network to directly estimate the latest space variables from backscatter data collected by the sensor. This method can produce real time imagery without directly solving Maxwell's equation. In the next period, we will study methods for enhancing the contrast image. This activity is in support of our goal in Aim 2 which is creating signal processing architectures to support biomarker computations on resource-constrained, high data rate sensor arrays.

[1] Civek, Burak C., and Emre Ertin. "Bayesian Sparse Blind Deconvolution Using MCMC Methods Based on Normal-Inverse-Gamma Prior." IEEE Transactions on Signal Processing 70 (2022): 1256-1269. NIHMS1839071.

[2] Civek, Burak C., and Emre Ertin."MCMC Methods for Estimation of Thoracic Fluid Levels using UWB Radar,." Poster at IEEE BHI-BSN 2022.

B.2.1.3. - Activity 1.3 (Aim 2): *Development of the next generation of the MotionSense HRV platform as a reference implementation of micromarker abstractions for PPG and IMU signals*

TR&D3 specific objectives include development of reference designs and associated software development kits to put techniques to develop and disseminate micromarker based biomarker implementations with built-in controls to explore privacy-utility tradeoff. The new learning techniques we explore under Aim 1 and 2 require embedding of the ML architectures such as deep nets, autoencoders on the edge devices. Towards this end, we have developed a dual-core version of our wristband and rewrote the software stack from the ground up to support common machine learning abstractions often encountered in bio/micromarker implementations. We performed detailed analysis on techniques for optimizing the model and memory utilization of the deployed model in the system. The firmware was further modified to be backward compatible with the previous version of the firmware by modifying the packet format used in data transfer. The activity-related measure termed ENMO (Euclidean norm minus one) is also implemented on the sensor firmware, which serves as a measure for activity level.

B.2.1.4. - Activity 1.4 (Aim 2): *Scalable sensing/computing substrates for near field RF array Imaging*

We developed a multiple transmit-receive radar system using two phase-locked loop systems (Transmit PLL and reference PLL) to generate frequency sweeps in the frequency band of 500 MHz to 6 GHz that is suited for interrogating biological tissues. The RF section of the system comprises mixer circuitry that combines the received RF signal with the reference signal to recover the frequency response of the region of interest. The RF system is interfaced with a digital section that samples and digitizes the received signal and combines the multi-channel measurements from different transmit-receive pairs to infer the underlying tissue profile's electrical properties such as permittivity and conductivity. The system is paired with an antenna that is matched to the tissue profile under investigation. The antenna is fabricated on a flexible substrate to obtain conforming array systems.

The radar system will be applied to imaging and sensing the cardiac muscle movement to assess the contractility strength by utilizing multiple array elements covering the thoracic cavity. The radar system will also be utilized in estimating the lymphatic fluid level in the limbs of people and monitor the progression of Lymphedema. The current activity involves designing the antenna to scale for different applications, designing a matching medium to maximize the energy coupled to the tissue of interest, and designing a cyber-physical system to facilitate the computation of task-specific micromarker.

B.2.1.5. - Activity 1.5 (Aim 1): *Platform-aware machine learning for low-end IoT devices*

With their considerable superior accuracy, robustness, and generalizability relative to traditional machine learning methods, deep neural networks have gained rapid adoption for processing sensory data. However, they also create the challenge of efficient computation on low-resource devices. In this activity, working in close cooperation with researchers from Arm, which designs the most prevalent embedded processors used in wearable devices, we developed and released THIN-Bayes, an open-source software tool for neural architecture search for wearable devices employing resource-constrained microcontrollers. THIN-Bayes, which we presented at the tinyML Summit 2022 (Saha, et. al., 2022a[3]), makes use of hardware-in-loop with bayesian optimization. It is based on a fast, parallel, and gradient-free Bayesian optimizer called MANGO which we also developed with Arm. THIN-Bayes enables lightweight models for challenging applications on low-end platforms with arbitrary optimization parameters. We also applied THIN-Bayes to two scenarios of on-device computation: human activity classification and head-pose estimation using earable sensors (Auritus; Saha, et. al., 2022b[4]), and 3D motion trajectory tracking using on-body wearables (TinyOdom; Saha, et. al., 2022c[5]). In both cases, the THIN-Bayes approach has produced neural architectures that fit within ultra-resource constrained platforms while meeting real-time latency requirements and significantly advancing the performance relative to the state-of-the-art models. As part of Auritus, we also collected and released a carefully annotated open-source dataset with 2.43 million inertial samples related to head and full-body movements, consisting of 34 head poses and nine activities from 45 volunteers.

[3] a. Saha, Swapnil Sayan, Sandeep Singh Sandha, Mohit Aggarwal, and Mani Srivastava. "THIN-Bayes: Platform-Aware Machine Learning for Low-End IoT Devices." Poster at the tinyML Summit 2022.

[4] b. Saha, Swapnil Sayan, Sandeep Singh Sandha, Siyou Pei, Vivek Jain, Ziqi Wang, Yuchen Li, Ankur Sarker, and Mani Srivastava. "Auritus: An Open-Source Optimization Toolkit for Training and Development of Human Movement Models and Filters Using Earables." Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies 6, no. 2 (2022): 1-34. NIHMS1839165

[5] c. Saha, Swapnil Sayan, Sandeep Singh Sandha, Luis Antonio Garcia, and Mani Srivastava. "Tinyodom: Hardware-aware efficient neural inertial navigation." Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies 6, no. 2 (2022): 1-32. NIHMS1839164

B.2.1.6. - Activity 1.6 (Aim 3): *Characterizing user re-identification risks from wrist-worn accelerometry data*

The aim of this activity is to characterize the privacy risks arising from sensor data in wrist-worn devices, particularly motion data, that is shared with downstream data consumers for biomarker prediction and interventions. During Year 1, we had reported privacy risks that arose from sharing raw IMU sensor measurements as well as controlling privacy-utility trade-off via adversarial perturbation. Of note, during Year 2 we presented a paper (Saleheen, et. al., 2021[6]) based on that work at ACM CCS 2021, which is one the top conferences in computer and communication security. Our focus during Year 2 was on understanding and quantifying privacy risks from sharing *processed* sensor data as would be the case with wearable sensors with local low-power computing resources that would allow mapping a sequence of raw sensor measurement sequence to a sequence of higher semantic value data products such as inferences, micromarkers, engineered features, and embeddings (e.g., using task-aware autoencoder based neural data compression that we introduced last year). In particular, we investigated privacy risks from two forms of processed motion sensor data: time series of human activity labels and time series of step counts. As human activity labels and step counts are computed over windows of IMU sensor measurements, the processed data are much more coarse-grained in both the temporal dimension (lower frequency) and the value dimension (categorical and small integers as opposed to real-valued). We are exploring two research questions: (Q1) How much reidentification potential is present in different inferences? and, (Q2) Which contexts contribute more towards an increase of re-identification risks?

[6] Saleheen, Nazir, Md Azim Ullah, Supriyo Chakraborty, Deniz S. Ones, Mani Srivastava, and Santosh Kumar. "WristPrint: Characterizing User Re-identification Risks from Wrist-worn Accelerometry Data." In Proceedings of the 2021 ACM SIGSAC Conference on Computer and Communications Security, pp. 2807-2823. 2021. NIHMS1839082

B.2.1.7. - Activity 1.7 (Aim 3): *Understanding factors behind privacy perception of IoT sensors*

An alternative to wearable sensors are ambient sensor devices which also allow for biomarker computation and delivery of interventions, e.g. digital assistants, wireless IoT sensors, etc. Besides alleviating the need for carrying a device in person, they allow biomarker monitoring for multiple individuals in a space, easier instrumentation, and more comfort. Such instrumentation in private and personal spaces has led to different kinds of growing concerns regarding privacy. The existing notion behind privacy is that the sensors whose data can easily be understood and interpreted by humans (such as cameras) are more privacy-invasive than sensors that are not human-understandable, such as RF (radio-frequency) sensors. However, given recent advancements in machine learning, we can not only make sensitive inferences on RF data but also translate between modalities. Thus, the existing notions of privacy for IoT sensors need to be revisited. To understand the privacy implications, we conducted an online study of 122 participants from the USA to find what factors affect the privacy perception of a user regarding a device or a sensor.

B.2.1.8. Summary of Push-Pull Activities with CPs

CP1 (Nahum-Shani): The Mobile-Assistance for Regulating Smoking (MARS) project drafted the protocol for the study, where MotionSense sensors will be used to assess the smoking state and HRV as a measure of self-regulatory capacity. We used the study protocol to inform micromarker abstractions required to support the study objectives while minimizing latency and data rates to mobile devices. We are in the process of transitioning this study to the new MotionSense HRV platform.

CP3 (Klasanja): If ongoing Activity 1.5 shows that steps data has reidentification potential, it may inform CP3 of privacy risks as it collects physical activity and steps data in up to one year-long study.

CP6 (Inan): We continued to have discussions with Dr. Inan over the role of micromarkers in assessing cardiac state using signals from ballistocardiography and seismocardiography. With Dr. Inan's group, we are exploring the use of RF arrays in the motion capture of cardiac muscle as a complementary sensor modality to ballistocardiography.

CP7 (Ives): The work of Activity 1.5 denotes the privacy risk from publicly sharing wrist-worn accelerometry data that may be applicable when CP7 begins the work of publicly releasing the data being collected in the MOODS study where participants collect stress and activity data from wrist-worn Fossil smartwatches for up to 100 days and have provided consent for publicly releasing their data to advance research in identifying sources of stress from wearable sensor data.

B.2.2. Specific Objectives

TR&D3 will develop, validate, and disseminate algorithms, tools, and software/hardware designs for the translation of temporally-precise mHealth interventions through the resource efficient, real time, low-latency, and privacy-aware implementation of an array of digital biomarkers that can be deployed at scale. Our approach is centered around a hierarchical computing framework that reduces the data into minimal modular abstractions called Micromarkers computed on the edge devices. TR&D3 will provide the research community with 1) mDOT Center applications and software development kits (SDK) on popular wearables, personal devices, and smartphones with embedded micromarker based implementation of biomarkers of stress, fatigue, speaking, smoking, craving, eating, brushing, and new biomarkers from CPs; 2) Reference design and prototypes of mDOT Center radio-frequency (RF) Patch sensors, modular hardware modules, and embedded software cores to power wearable sensor arrays; 3) Toolbox for exploring privacy implications of sensor and biomarker choices and enabling run-time control over privacy-utility trade-off in biomarker implementations. These tools will enable continuous, high throughput, low-latency capture of current and emerging biomarker streams to support large-scale, long-term research studies that provide privacy management at the entire lifecycle, including study design, data collection, and data sharing.

B.2.3. Significant Results (including major findings, developments, or conclusions both positive and negative)

B.2.3.1 - Activity 1.1: Our findings on prototype implementation of the mircomarker framework on the MotionSense HRV platform show that with only 0.6% CPU utilization the micromarker framework show that PPG data can be compressed into micromarkers with low latency of 50 msec while retaining virtually identical performance (as compared to uncompressed data) in tachogram signal estimation.

B.2.3.2 - Activity 1.2: Our preliminary findings in this activity show that backscatter data from BioRF sensor have sufficient information content to obtain contrast images of the internal tissue profiles. This tissue profiles care inform care decisions in congestive heart failure and lymphedema use cases.

B.2.3.3 - Activity 1.3: Our findings from our prototype implementation show that micromarker framework and classical feature extraction methods (e.g. ENMO activity measures) can coexist in our edge device platform MotionSense HRV, that allows multimodal sensor data to be transformed into biomarkers of interest that can support multiple applications such as stress inference, gesture and activity recognition.

B.2.3.4 Activity 1.4: We have shown that the proposed integrated RF-digital substrates allow implementation of scalable 2D BioRF sensor arrays that can be tailored to different applications. The design can be manufactured using standard semi-flex PCB technology, making it possible to support large scale studies. Local digitization of the signals at each sensor allows the array size to scale with no penalty on latency and signal to noise ratio.

B.2.3.5. - Activity 1.5: The THIN-Bayes tool, the underlying MANGO Bayesian hyperparameter optimizer, and the Auritus and TinyOdom frameworks built using THIN-Bayes demonstrate levels of performance that far outperform the state of the art. For example, TinyOdom reduces the size of neural inertial models by 31× to 134× with 2.5m to 12m error in 60 seconds, enabling the direct deployment of models on URC devices while still maintaining or exceeding the localization resolution over the state of the art. Likewise, Auritus recognizes activities with 91% leave 1-out test accuracy (98% test accuracy) using real-time models as small as 6-13 kB. Our models are 98-740x smaller and 3-6% more accurate over the state of the art. We also estimate head pose with absolute errors as low as five degrees using 20kB filters, achieving up to 1.6x precision improvement over existing techniques.

B.2.3.6. - Activity 1.6*:* Preliminary findings from the research on quantifying reidentification risks from sharing processed motion sensor data suggest that modern machine learning methods allow reidentification to be done successfully when temporal characteristics are retained.

B.2.3.7. - Activity 1.7: Our findings from the 122-person study on the factors that affect the privacy perception of a user regarding a device or a sensor show that a user’s perception of privacy not only depends upon the data collected by the sensor but also on the inferences that can be made on that data and familiarity with the device and its form factor as well as the control a user has over the device design and its data policies. When the data collected by the sensor is not human-interpretable, it is the inferences that can be made on the data and not the data itself that users care about when making informed decisions regarding device privacy.

B.2.4. Key Outcomes & Other Achievements

In collaboration with Arm, UCLA created MANGO, a fast, parallel, and gradient-free Bayesian optimizer, and THIN-Bayes, a platform-aware machine learning tool for low-end IoT devices that utilizes MANGO. Further, we created two frameworks that use THIN-Bayes to specifically target resource-efficient neural models for human activity classification and head-pose estimation using wearable sensors (Auritus), and 3D motion trajectory tracking using on-body wearables (TinyOdom).

TR&D3 - Translation	Books	Papers	Abstracts
Number Published	0	5	2
Number in Press	0	1	0
Number in Submission/Review	0	3	0

B.4. What opportunities for training and professional development has the project provided?

During Y2, at UCLA the project activities partially engaged three Ph.D. students, two undergraduate students, and one postdoctoral researcher (some of these were funded via synergistic funding). The project has furthered their educational training by giving them hands-on experience on various facets of sensor information processing towards biomarker computation on resource-constrained wearable devices, and on quantifying and mitigating privacy risks. Additionally, the research in the project was also incorporated into two graduate courses via special lectures, assignments, and projects, resulting in influencing the training of 50+ students in the ECE and CS Departments.

During Y2, at OSU the project activities partially engaged three Ph.D. students, two undergraduate students, and one research engineer (some of these were funded via synergistic funding). The project gave the students the opportunity to work on an interdisciplinary project that combines elements of sensor hardware design, machine learning algorithm development and embedded computing. Furthermore, a design project and examples from RF based biomedical sensing and a design project have been incorporated into a senior level undergraduate course providing training to 25 students in the ECE and CS departments.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS Not Applicable
C.2 WEBSITE(S) OR OTHER INTERNET SITE(S) Not Applicable
C.3 TECHNOLOGIES OR TECHNIQUES NOTHING TO REPORT
C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES Not Applicable
C.5 OTHER PRODUCTS AND RESOURCE SHARING NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

A. COMPONENT COVER PAGE

Project Title: mDOT Training and Dissemination
Component Project Lead Information: SHETTY, VIVEK

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mHealth Center for Discovery, Optimization & Translation of Temporally-Precise Interventions (the mDOT Center) will enable the new paradigm of temporally-precise medicine to maintain health and managing the growing burden of chronic diseases. The mDOT Center will develop and disseminate the methods, tools, and infrastructure necessary for researchers to pursue the discovery, optimization and translation of temporallyprecise mHealth interventions. Such interventions, when dynamically personalized to the moment-to-moment biopsychosocial-environmental context of each individual, will precipitate a much-needed transformation in healthcare by enabling patients to initiate and sustain the healthy lifestyle choices necessary for directly managing, treating, and preventing medical conditions. Organized around three Technology Research & Development (TR&D) projects, the mDOT Center will generate multiple technological innovations and translate them into a unique national technological resource for the mHealth community in the form of easily deployable wearables, apps for wearables and smartphones, and a companion mHealth cloud system, all open-source.

Given that the inherently transdisciplinary, team-based nature of mHealth research requires scientists to cross disciplinary and institutional boundaries, training and dissemination in mHealth technologies requires a team-science approach. The mDOT Center will leverage our established and mature infrastructure, widely visible mHealthHUB platform, and an experienced team to develop training and dissemination activities that extend beyond the CPs and SPs to involve new research groups with little or no technological expertise. By reducing access barriers, we seek to reduce the growing disparity among various research groups in using latest mHealth sensing, biomarker, and analytics technology in their research. The main goals of the mDOT Center's Technology Training and Dissemination (TT&D) Core are two-fold: (a) improve the general understanding and uptake of the mDOT Center technologies and methods by the mHealth research communities; (b) develop a perpetuating cadre of transdisciplinary researchers conversant with the mDOT Center technologies and able to effectively apply them in their own research programs.
Envisioned as national resource, the dissemination activities of the mDOT Center will focus on informing the scientific community about the tools and processes developed by the mDOT Center and facilitate broad distribution and optimized use of the mDOT Center technologies. The mDOT Center will use the Theory of Action (described below) as an organizing framework for its key training and dissemination activities to achieve the outcome objectives of the TT&D Core. Training efforts will reach beyond mDOT Center affiliates to include mentorships, a scholar exchange program, and a visiting scholar residency program. Our annual mHealth Training Institute (mHTI) and other group courses and workshops are common forums that will blend the mDOT Center's dissemination with direct training activities. Dissemination activities include the hosting of our community website (mHealthHUB; https://mhealth.md2k.org/), development of user application documentation, delivery of virtual seminars, publication of research methods and findings, development of the user community, and technology transfer. The TT&D core will pursue the following specific aims:

Aim 1: [Training] Provide direct training activities that leverage annual workshops, conferences, and meetings of professional societies, and conduct an annual mHealth training institute to develop a perpetuating cadre of outside researchers well-equipped to apply the mDOT Center technologies and methods.

Aim 2: [Dissemination] Provide “light-touch” outreach using web-portals with “heavy-touch” outreach activities including training sessions, workshops, and conferences to inform the scientific community about the technical capabilities and accomplishments of the mDOT Center, and to both promote and enable a broader use of the mDOT Centermethods and technologies.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The results of the advanced quantitative methods studying the formation of transdisciplinary teams and the development of team processes during the mHTIs have been published in prominent peer-reviewed, open-access, scientific journals with high impact factor (a) Journal of Clinical and Translational Science and (b) PLOS One.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

B.6.1. - Write up and publish the analysis of the 2022 mHTI to advance Team Science.

B.6.2. - Organize and conduct the 2022 mHTI.

B.6.3. - Reorganize the mHealthHUB portal and website.

B.6.4. - Continue with online webinars.

B.6.5. - Deploy the CTSI/Vanderbilt-developed Flight Tracker software to automate tracking and analysis of career outcomes, including transdisciplinary collaborations, publications, funding, training activities, and other milestones of the mHTI scholars.

B.6.6. - Utilize the longitudinal data to analyze the short-term and long-term causal effects of the mHTI on the mHTI scholars' academic collaboration for journal papers and grant writing with other mHTI and/or non-mHTI scholars. We plan on two types of causal evaluations: (1) evaluate the value-add of the mHTI by assessing within-person changes over time using the difference-in-difference design; (2) evaluate the impact of the mHTI program using a quasi-experimental design by comparing mHTI scholars and non-scholars with similar background characteristics regarding their collaboration activities.

B.2 What was accomplished under these goals?

In Year 2, the Training and Dissemination Core undertook a variety of activities (as described below) to fulfill its goals.

B.2.1. - Activity 1 (Aim 2): *Training*
Due to the ongoing COVID pandemic, the training activities were conducted virtually.

The main focus of the training was the development and conduct of a virtual version of the annual mHealth Training Institute (mHTI). This entailed deployment of a virtual events platform (Zoom) and a comprehensive, online application management system (SmarterSelect). The training activities were augmented by the participation of the CERES (Connecting the EdTech Research Ecosystem) collaborative; a UC-Irvine based Center dedicated to training and developing research ways to reduce widening disparities in learning and development due to unequal access and personalization of digital technology across populations and contexts (https://ceres.uci.edu/). From a pool of 232 applicants, 30 were chosen as scholars for the 2022 mHTI. A corresponding group of faculty, comprising both academics and NIH Program Officers was also recruited. The virtual 2022 mHTI was conducted between May 2 and July 28, 2022 (https://mhti.md2k.org/index.php/program/2022-program) and comprised of a series of core lectures and seminars as well as mentored team activities.

mDOT Center webinars: In addition to the mHTI-related lectures, the TT&D core conducted a series of webinars on themes of interest to the broader mDOT Center community. To increase the national and international impact of the mDOT Center, the webinar series has recruited faculty from institutions abroad, including the UK, Switzerland, and New Zealand.

B.1.2. - Activity 2 (Aim 1): *Dissemination*
To allow the didactic content of the 2022 mHTI to be broadly accessible, the 12 webinars/seminars were recorded and curated on the mHTI's website and YouTube channel as well as the mHealthHUB platform.

B.2.2. Specific Objectives

Given that the inherently transdisciplinary, team-based nature of mHealth research requires scientists to cross disciplinary and institutional boundaries, training and dissemination in mHealth technologies requires a team-science approach. mDOT will leverage its established and highly successful infrastructure, widely visible mHealthHUB platform, and deeply-experienced team to develop training and dissemination activities that extend beyond the collaborative projects (CPs) and service projects (SPs) to involve new research groups with little or no technological expertise. To achieve its goals, mDOT will pursue the following activities: Train a cadre of transdisciplinary mHealth scientists to develop national capacity; Answer a series of process (or implementation) and outcome (or impact) questions relative to the 2022 mHTI. The process evaluation questions investigate aspects of the design and implementation of the mHTI. Outcome evaluation questions focus on the extent to which intended goals were achieved; Use the mHTI as a testbed to apply advanced quantitative methods to study the formation of transdisciplinary teams and the development of team processes central to the effective functioning of highly diverse teams.

B.2.3. Significant Results

Table 1. Background Characteristics of 2022 mHTI Scholars

	N	%
Race/Ethnicity (participants could select multiple)	27	100
White/Caucasian	17	62.96
Asian	9	33.33
Hispanic/Latino/Latina	2	7.41
Black/African American	2	7.41
Gender	27	100
Female	20	74.07
Male	7	25.93
Region	28	100
Northeast	15	55.56
Midwest	5	18.52
Southeast	2	7.41
West	2	7.41
Southwest	3	11.11
Institution Type	27	100
University	20	74.07
Hospital or Clinic	7	25.93
Discipline	27	100
CS/Engineering/Data Science	7	25.92
Medicine/Nursing	4	14.81
Psychology	11	40.74
Public Health/Others	5	18.52
Stage	27	100
Postdoc or other early career	4	14.81
Assistant or associate professor or other mid-career	21	77.78
Full professor or other late career	1	3.70
Other	1	3.70

To evaluate the process and outcomes of the 2022 virtual mHTI program, we disseminated a number of surveys during the program. By every metric, the 2022 mHTI was very impactful.

Fig.1 shows that the 2022 mHTI scholars' mHealth research recognition (mHR) and self-efficacy (EFF) significantly increased between pre- and post-mHTI (p <0.0001).

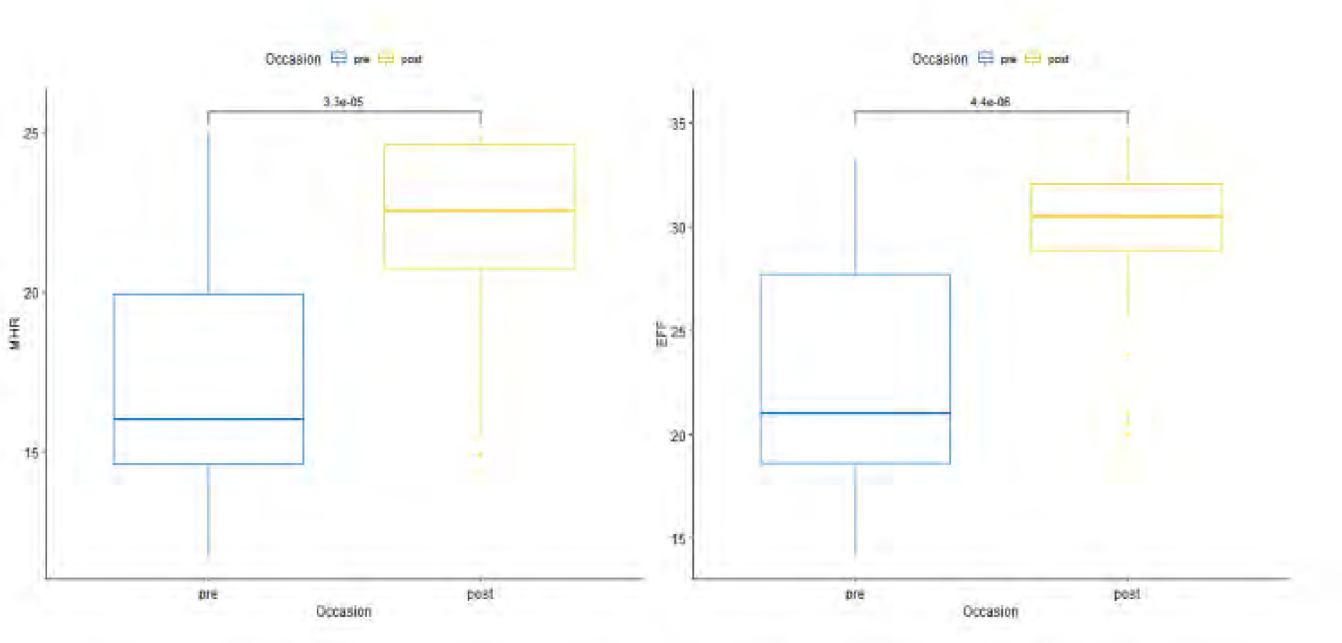

Fig. 1: Pre- and post- mHTI comparison on scholars' mHealth research recognition (MHR) and self-efficacy (EFF) . Blue indicates the pre-institute scores, and yellow indicates the post-institute scores. The number on the top bar indicates the p-value from the t-test on the pre- and post-mHTI differences for MHR (left) and EFF (right).

Table 2 summarizes the 2022 mHTI scholars' overall experience with the institute. The majority of the participants responded that the 2022 virtual mHTI was "extremely worthwhile" [mean score = 6.39 (out of 7) with SD of 0.79 (N=28)]. Overall, the 2022 scholars were highly satisfied with their experience of the team-based project, networking opportunities, and organization of the institute.

Table 2. 2022 mHTI scholars' overall experience of mHealth Training Institute

Item	Mean	SD	Out of
Overall, was the virtual mHealth Training Institute worthwhile for you?	6.39	0.79	7, Extremely worthwhile
Overall experience of team-based projects as an opportunity to ...			
* apply material from the training sessions/presentations	4.39	0.83	5, Extremely Positive
* get to know other mHTI scholars	4.29	0.66	5, Extremely Positive
* get to know the mHTI faculty mentors	4.21	0.96	5, Extremely Positive
* learn about mHealth project development	4.39	0.92	5, Extremely Positive
* learn about working on a multidisciplinary team	4.50	0.69	5, Extremely Positive
Satisfaction with the quality of the following networking opportunities to ...			
* be exposed to ideas and perspectives of mHTI scholars/faculty from other specializations/disciplines	3.18	0.77	4, Excellent
* receive input and feedback on your ideas or work	3.11	1.03	4, Excellent
* interact with peers from other specializations/disciplines during completion of tasks related to the workshop	3.18	0.9	4, Excellent

Table 3 lists the 2022 mHTI scholars' pre- and post- evaluation of the comfort level with the topics addressed in the pre-institute lectures. The scholars' comfort levels with each topic significantly increased after taking the pre-institute lecture.

Table 3. 2022 mHTI scholars' comfort levels with the lecture topics before- and after taking each lecture

Lecture Topics	Before	After	Difference
Frameworks for Developing Behavioral Interventions	2.61	3.85	1.26*
System Dynamics and Bayesian Modeling as Groundwork for Behavioral Interventions	2.52	3.31	0.79*
Developing and Implementing Behavioral Intervention Technologies	3.25	4.18	0.93*
Case Studies of Progression through Stages of Behavioral Intervention Development	2.97	4.07	1.10*
Aligning Community, Population, & Digital Health to Produce Agile Actionable Real World Evidence	2.82	3.46	0.64*
Data Missingness in mHealth Research	2.86	3.68	0.82*
ePlatforms for Implementing mHealth Studies	3.21	4.07	0.86*
Social Network Analysis in mHealth	2.79	3.81	1.04*

*Notes: the scores were reported by scholars to evaluate their levels of comfort working with the lecture content before and after the lecture session. 1 = Very uncomfortable, 5 = Very comfortable. * denotes the difference is statistically significant at the significant level of 0.01.*

B.2.4. Key Outcomes & Other Achievements

B.2.4.1. - The educational consultant (Dr. Jeon) used the mHTI to conduct a longitudinal social network analysis of the scholars' communications during the mHTI programs. Their findings have been summarized by a paper that was published in the *Journal of Clinical and Translational Science*, a top-tier journal in the team science field.

B.2.4.2. - A second paper has recently been accepted for publication at PLOS ONE. In this paper, we applied stochastic actor-oriented models (SAOM) to understand how the mHTI interactions among scholars may have influenced scholars' sense of team psychological safety and vice versa. Our findings suggest the presence of some social selection along with homophily effects - in certain years of the Training Institute, scholars were likely to communicate with others from the same team or discipline while also choosing to communicate with those who had more dissimilar team psychological safety. Fig. 2 illustrates the scholars' project-based communications.

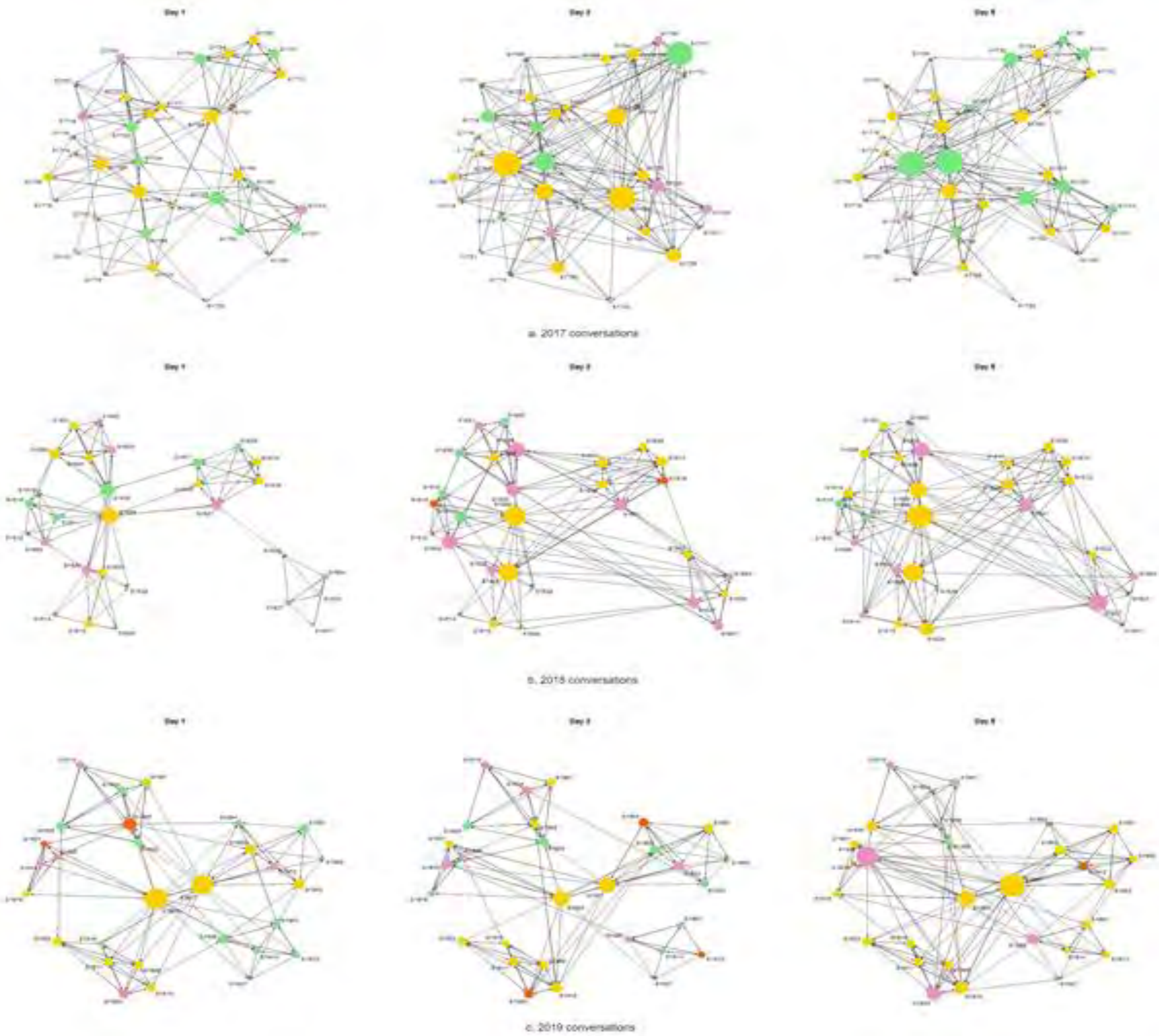

Fig. 2: Scholars' conversation network graphs with behavior homophily. Pink represents low scores, green represents medium scores, yellow represents high scores, and red represents missing scores (NA).

B.4. What opportunities for training and professional development has the project provided?

B.4.1. *- mHTI-related*: The project provided the opportunity for training and professional development of three doctoral students in education: Jinwen Luo (fourth-year Ph.D. student in Quantitative Methods), Eric Ho (fourth-year Ph.D. student in Quantitative Methods), and Minho Lee (third-year Ph.D. student in Quantitative Methods). The three students played a major role in the development, implementation, and data analysis of the 2022 mHTI program survey under the direction of Dr. Jeon (assessment consultant). In particular, Luo, Ho, and Lee served as three main authors of the two journal papers that we listed as Key Outcomes (Section B.2.4).

B.4.2. *- CP2*: The Personalized Digital Behavior Change Interventions to Promote Oral Health project has provided for the training of two graduate students (Anna Trella and Kelly Zhang) working under the supervision of TR&D2 PI Susan Murphy.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. COMPONENT PARTICIPANTS

Not applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? Not Applicable
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? NOTHING TO REPORT
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

The COVID pandemic has prevented the initiation of ‘in-person” activities. With conditions stabilizing, we plan to transition to in-person activities in 2023 and beyond.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subject

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable