Detection and Monitoring of Viral Infections via Wearable Devices and Biometric Data - Supplemental Information

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1. SUPPLEMENTAL INFORMATION

1.1. Reproducibility and Replicability

There are several online platforms aimed at connecting researchers to encourage collaboration and resource sharing in the field of digital medicine. For instance, the Digital Biomarker Discovery Pipeline provides code for wearable data processing and digital biomarker discovery (1). The Digital Health Data Repository (DHDR) curates datasets in the digital health space and includes sample data for use with the DBDP. The aim of the DBDP is to provide all resources for digital biomarker discovery to facilitate collaborations and transparency for wearable data analysis (1). There have been increasing partnerships between research groups and commercial manufacturers to explore the utility of BioMeTs for detecting stress, ILI, and COVID-19 (2). This allows researchers access to a much larger dataset and for manufacturers to extend device utility. Increasing transparency and openness by making data and code openly available is increasingly being adopted to improve replicability. The DBDP is the first comprehensive platform for open-source, end-to-end digital biomarker development (3). This will enable researchers to verify published results and to conduct alternative analyses, thereby also extending the utility of collected data. Several efforts like the All of Us Research Program, the DHDR, the UCI Machine Learning Repository, Physionet, and MHEALTH make datasets available for use by other researchers.

1.2. Data Privacy

There have been several efforts to ensure security of patient data from biometric monitoring technologies (BioMeTs) (4). However, considerable gaps exist in the protection of medical and personal health information which will have to be addressed as BioMeTs become more widely used in healthcare. Concerns regarding the use of wearables and sensors in healthcare include ethical, legal, data security, infrastructure, and regulatory risks (5). Lack of technical expertise required to safeguard personal device data can pose a data security risk. Since most research studies require individuals to operate their consumer BioMeTs themselves, these studies need to ensure that users understand the best practices to safeguard their data.

Transmission between BioMeTs and data storage are both prone to security threats. Rigorous measures need to be put in place to ensure data security at all levels, especially due to the current lack of governance and guidelines safeguarding BioMeT data collection. The Health Insurance Portability and Accountability Act (HIPAA) was put in place to ensure protection of health information, and the HIPAA security rule requires specific protections to safeguard electronic health. Similar guidelines need to be established for secure storage and sharing of information collected from BioMeTs. Standard guidelines would ensure compliance from all research groups and improve security measures for data storage. Secure data storage and sharing standards for digital health data are essential to advance the use of BioMeT-informed decisions in clinical care.

The fact that BioMeTs collect a host of personal data pertaining to location, health status, and lifestyle raises questions regarding data privacy (6). Anonymization, or techniques to protect individual privacy in databases storing personal information by deleting identifiable information such as names, addresses, telephone numbers, and social security numbers, are usually employed to safeguard user information. The digital health field is still in the process of defining methods to anonymize data and to understand whether true de-identification without the possibility of re-identification is a realistic goal (7, 8). To preserve trust from consumers, patients, and research participants, secure data storage and sharing standards for digital health data are essential. More research is needed to determine if current de-identification practices are adequate or whether novel solutions are required to protect user identities.

Ensuring research study participant understanding of privacy concerns is necessary and must be conveyed through informed consent. Although BioMeTs might collect personal data only after users agree and sign consent forms, most users provide consent without a thorough understanding of what the legal agreements entail. Employing BioMeTs for measuring outcomes in clinical studies must involve a complete user understanding of associated risks and benefits. An informed consent ensures that the participants comprehend all the information correctly and can make an autonomous decision. Concerningly, there are still unresolved legal issues to be tackled in this field. The extent of coverage of Certificates of Confidentiality for data collected from personal digital devices is an example. Appropriate efforts must be undertaken to provide all the information required to make an informed decision by employing tools like audio-visual aids, assessment of patient comprehension, extended discussions between participants and the research team, and study brochures (9). In the field of genetics, genetic counselors help patients navigate the consent process by providing information and offering guidance. Similarly, a digital medicine counselor who possesses expertise in digital data could guide individuals through the potential benefits and risks of contributing BioMeT-collected data for research purposes. This would also boost public confidence in research studies by helping participants navigate all their concerns with the right information. Enabling participants to understand the potential risk of loss of privacy with such studies is an important part of ensuring truly informed consent.

1.3. Population Data for Viral Illness Epidemiology

Supplemental Table 1: Population-level viral illness information via BioMeTs data - real world evidence

	Viral Illness	**Features Analyzed**	**BioMeT(s)**	**Population Size**	**Key Findings**
Radin Fitbit Analysis (10)	Influenza	HR, Sleep, Activity	Fitbit	60,473	Individuals with a weekly mean HR 0.5 SD[1] above their yearly average and weekly activity 1.0 SD less than their average correlated with local CDC[2] ILI[3] rates
Scripps' Fitbit Study (11)	Influenza	HR, Sleep	Fitbit	47,249	The weekly proportion of users with anomalous Fitbit data significantly improved models using CDC ILI data from three weeks prior to predict current ILI at the state level in the US
Corona Data Donation App (12)	COVID-19	HR, Activity	Multiple wrist BioMeTs	538,010	BioMeTs data correlated with local COVID-19 case counts in Germany

[1]Standard deviation
[2]Centers for Disease Control and Prevention
[3]Influenza-like illness

Huami Users (13)	COVID-19	HR, Sleep	Huami BioMeTs	1.3 million	Physiological anomalies, defined as a resting HR 1.5 SD above a person's normal or sleep longer than 0.5 SD below normal, correlated with COVID-19 case counts in Chinese cities
Twenty Country Lockdown Impact in Oura Ring Users (14)	COVID-19 (effect of lockdowns)	HR, Sleep	Oura Ring	113,000	Stricter lockdowns were associated with delayed mid-sleep times, with decreased variability and resting HR

1.4. BioMeT Data for Individual Diagnosis and Prognosis

Supplemental Table 2: Individual-level diagnosis and/or prognosis of viral illness via BioMeT data

	Viral Illness	**Features Analyzed**	**BioMeT(s)**	**Population Size (Number of Cases)**	**Key Findings**
Evidation Achievement App (15)	Influenza	HR, sleep, activity	Multiple wrist BioMeTs	9,495 with data	Changes in sleep, activity and HR correlated with self-reported symptoms consistent with ILI.
TemPredict (16)	COVID-19	Skin temp., HR, RR, HRV	Oura Ring	50 (50)	Individual elevations in peripheral temperature correlate with self-reported fever.

Stanford COVID-19 Wearables Study (17)	COVID-19	HR, sleep, activity	Fitbit, Apple Watch, Garmin, and other	5,262 (32)	Most COVID-19 cases had changes in their HR, steps or sleep. Two-thirds could have potentially been detected pre-symptoms onset.
Fitbit Study (18)	COVID-19	HR, activity, RR, HRV, sleep	Fitbit	187,573 (2,745)	HR and RR are typically elevated, and HRV reduced in those with infection and can help in its prediction.
Stanford Real-Time Alerting Study (19)	COVID-19	HR	Fitbit, Apple Watch, Garmin and other	2,112 with data (68)	Alerts were generated a median of 3 days prior to symptoms in the majority of COVID-19 cases, but also other infections and non-infection events.
DETECT (20)	COVID-19 & other viral respiratory infections	RHR, sleep, activity	Data from Fitbit and any Apple HealthKit- or Google Fit-connected BioMeT	30,529 (54)	BioMeT data can significantly improve symptom-only based models to predict COVID-19 positivity.
Whoop System (21)	COVID-19	RR, RHR, HRV	WHOOP	271 (81)	Changes in sleeping RR identified a minority of COVID-19 positive cases in 2 days prior to symptom onset.

Evidation (22)	COVID-19, Influenza	RHR, activity, sleep	Fitbit	6,926 (1,311 Influenza, 41 COVID-19 with data)	BioMeT data showed similar magnitudes in daily changes of steps and HR for both influenza and COVID-19 cohorts
Warrior Watch Study (23)	COVID-19	HRV	Apple Watch	297 (48)	HRV metrics can help identify individuals with COVID-19 and related symptoms.
CovIdentify (24)	COVID-19, Influenza	RHR, sleep, activity	All Apple HealthKit-connected BioMeTs	7501 (80 COVID-19; 116 Influenza)	Increased RHR and decreased Steps 3-5 days prior to test. Reported demographic imbalances in BYOD studies.
DeCODe (25, 26)	COVID-19	Multiple features	VitalPatch	Plans for 1600 with 400 in phase 1 and 1200 in phase 2	All participants COVID-19 positive. Wearable patch data and analytic engine to identify early signs of decompensation requiring hospitalization.

LITERATURE CITED

1. Digital health data repository (dhdr), jul 2021.
2. Can your garmin detect coronavirus?, April 2020. Publication Title: Garmin Blog.
3. B. Bent, K. Wang, E. Grzesiak, C. Jiang, Y. Qi, Y. Jiang, P. Cho, K. Zingler, F.I. Ogbeide, A. Zhao, R. Runge, I. Sim, and J.P. Dunn. The digital biomarker discovery pipeline: An open-source software platform for the development of digital biomarkers using mhealth and wearables data. *Journal of Clinical and Translational Science*, 5(1), 2021.
4. B. Woods, A. Coravos, and Joshua D. Corman. The case for a hippocratic oath for connected medical devices. *Journal of medical Internet research*, 21(3):e12568, 2019.
5. E.S. Izmailova, J.A. Wagner, and E.D. Perakslis. Wearable devices in clinical trials: Hype and hypothesis. *Clinical Pharmacology and Therapeutics*, 104(1):42–52, jul 2018.
6. T. Jourdan, A. Boutet, A. Bahi, and C. Frindel. Privacy-preserving iot framework for activity recognition in personal healthcare monitoring. *ACM Transactions on Computing for*

Healthcare, 2(1):3:1–3:22, December 2021.

7. F. Lobelo, H. M. Kelli, S. C. Tejedor, M. Pratt, M. V. McConnell, S. S. Martin, and G. J. Welk. The wild wild west: A framework to integrate mhealth software applications and wearables to support physical activity assessment, counseling and interventions for cardiovascular disease risk reduction. *Progress in Cardiovascular Diseases*, 58(6):584–594, jun 2016.
8. L. Na, C. Yang, C. Lo, F. Zhao, Y. Fukuoka, and A. Aswani. Feasibility of reidentifying individuals in large national physical activity data sets from which protected health information has been removed with use of machine learning. *JAMA Network Open*, 1(8):e186040–e186040, dec 2018.
9. R.A. Kadam. Informed consent process: A step further towards making it meaningful! *Perspectives in clinical research*, 8(3):107, 2017.
10. J.M. Radin, G. Queer, and S.R. Steinhubl. Can Wearable Sensors Detect Influenza Epidemics? Correlation of Anomalous Fitbit Data with Influenza Surveillance Data. *Emerging Infectious Diseases*, 24(9):47, 2018.
11. J. M. Radin, N. E. Wineinger, E. J. Topol, and S. R. Steinhubl. Harnessing wearable device data to improve state-level real-time surveillance of influenza-like illness in the usa: a population-based study. *Lancet Digit Health*, 2(2):e85–e93, 2020.
12. Corona-Datenspende: https://corona-datenspende.de/science/en/, 2020.
13. G. Zhu, J. Li, Z. Meng, Y. Yu, Y. Li, X. Tang, Y. Dong, G. Sun, R. Zhou, H. Wang, K. Wang, and W. Huang. Learning from Large-Scale Wearable Device Data for Predicting Epidemics Trend of COVID-19. *Discrete Dynamics in Nature and Society*, 2020, 2020.
14. J.L. Ong, T. Lau, M. Karsikas, H. Kinnunen, and M. Chee. A longitudinal analysis of COVID-19 lockdown stringency on sleep and resting heart rate measures across 20 countries. *Scientific Reports 2021 11:1*, 11(1):1–11, jul 2021.
15. B. Bradshaw, K.J. Konty, E. Ramirez, W. Lee, A. Signorini, and L. Foschini. Influenza Surveillance Using Wearable Mobile Health Devices. *Online Journal of Public Health Informatics*, 11(1), may 2019.
16. B.L. Smarr, K. Aschbacher, S.M. Fisher, A. Chowdhary, S. Dilchert, K. Puldon, A. Rao, F.M. Hecht, and A.E. Mason. Feasibility of continuous fever monitoring using wearable devices. *Scientific Reports 2020 10:1*, 10(1):1–11, dec 2020.
17. T. Mishra, M. Wang, A.A. Metwally, G.K. Bogu, A.W. Brooks, A. Bahmani, A. Alavi, A. Celli, E. Higgs, O. Dagan-Rosenfeld, B. Fay, S. Kirkpatrick, R. Kellogg, M. Gibson, T. Wang, E.M. Hunting, P. Mamic, A.B. Ganz, B. Rolnik, X. Li, and M.P. Snyder. Pre-symptomatic detection of COVID-19 from smartwatch data. *Nature Biomedical Engineering*, 4(12):1208–1220, nov 2020.
18. A. Natarajan, H. Su, and C. Heneghan. Assessment of physiological signs associated with COVID-19 measured using wearable devices. *npj Digital Medicine 2020 3:1*, 3(1):1–8, nov 2020.
19. Arash Alavi, Gireesh K. Bogu, Meng Wang, Ekanath Srihari Rangan, Andrew W. Brooks, Qiwen Wang, Emily Higgs, Alessandra Celli, Tejaswini Mishra, Ahmed A. Metwally, Kexin Cha, Peter Knowles, Amir A. Alavi, Rajat Bhasin, Shrinivas Panchamukhi, Diego Celis, Tagore Aditya, Alexander Honkala, Benjamin Rolnik, Erika Hunting, Orit Dagan-Rosenfeld, Arshdeep Chauhan, Jessi W. Li, Caroline Bejikian, Vandhana Krishnan, Lettie McGuire, Xiao Li, Amir Bahmani, and Michael P. Snyder. Real-time alerting system for covid-19 and other stress events using wearable data. *Nature Medicine*, nov 2021.
20. G. Quer, J.M. Radin, M. Gadaleta, K. Baca-Motes, L. Ariniello, E. Ramos, V. Kheterpal, E.J. Topol, and S.R. Steinhubl. Wearable sensor data and self-reported symptoms for COVID-19 detection. *Nature Medicine 2020 27:1*, 27(1):73–77, oct 2020.
21. D.J. Miller, J.V. Capodilupo, M. Lastella, C. Sargent, G.D. Roach, V.H. Lee, and E.R. Capodilupo. Analyzing changes in respiratory rate to predict the risk of COVID-19 infection. *PLOS ONE*, 15(12):e0243693, dec 2020.

22. A. Shapiro, N. Marinsek, I. Clay, B. Bradshaw, E. Ramirez, J. Min, A. Trister, Y. Wang, T. Althoff, and L. Foschini. Characterizing COVID-19 and Influenza Illnesses in the Real World via Person-Generated Health Data. *Patterns*, 2(1), jan 2021.
23. R.P. Hirten, M. Danieletto, Lewis Tomalin, K.H. Choi, M. Zweig, E. Golden, S. Kaur, D. Helmus, A. Biello, R. Pyzik, A. Charney, R. Miotto, B.S. Glicksberg, M. Levin, I. Nabeel, J. Aberg, D. Reich, D. Charney, E.P. Bottinger, L. Keefer, M. Suarez-Farinas, G.N. Nadkarni, and Z.A. Fayad. Use of Physiological Data From a Wearable Device to Identify SARS-CoV-2 Infection and Symptoms and Predict COVID-19 Diagnosis: Observational Study. *Journal of Medical Internet Research*, 23(2), feb 2021.
24. P.J. Cho, J.J. Yi, E. Ho, Y.H. Dinh, A. Patil, L. Martin, G. Singh, M.H. Shandhi, B. Bent, G.S. Ginsburg, M. Smuck, C. Woods, R. Shaw, and J.P. Dunn. The demographic improvement guideline to reduce bias resulting from bring-your-own-device study design. *JMIR mHealth and uHealth*, Epub ahead of print, dec 2021. doi: 10.2196/29510.
25. K. Larimer, S. Wegerich, J. Splan, D. Chestek, H. Prendergast, and T. Van den Hoek. Personalized Analytics and a Wearable Biosensor Platform for Early Detection of COVID-19 Decompensation (DeCODe): Protocol for the Development of the COVID-19 Decompensation Index. *JMIR Research Protocols*, 10(5), may 2021.
26. D.M. Richards, M.J. Tweardy, S.R. Steinhubl, D.W. Chestek, T.L.V. Hoek, K.A. Larimer, and S.W. Wegerich. Wearable sensor derived decompensation index for continuous remote monitoring of COVID-19 diagnosed patients. *NPJ Digital Medicine*, 4(1):155, nov 2021.