November 17, 2022

H2O Therapeutics
% Yagmur Selin Gulmus-Kolay
CEO, H2O Therapeutics
Mustafa Kemal Mah. 2119. Sok. No 3 Bilkent
Cankaya, Ankara 06510
Turkey

Re: K220820
Trade/Device Name: Parky App
Regulation Number: 21 CFR 882.1950
Regulation Name: Tremor Transducer
Regulatory Class: Class II
Product Code: GYD, NXQ, ISD
Dated: October 13, 2022
Received: October 18, 2022

Dear Yagmur Gulmus-Kolay:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Patrick Antkowiak -S

for
Jay Gupta
Assistant Director
DHT5A: Division of Neurosurgical,
Neurointerventional
and Neurodiagnostic Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K220820

Device Name
Parky App

Indications for Use *(Describe)*
The Parky App is intended to quantify kinematics of movement disorder symptoms including tremor and dyskinesia, in adults (45 years of age or older) with mild to moderate Parkinson's disease.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

h2o therapeutics

510(k) Summary

1. **Submitter:**

H2O Therapeutics
Address: Mustafa Kemal Mah. 2119. Sok. No 3 Bilkent,
Çankaya, Ankara, 06510
Turkey
Contact Person: Ms. Yagmur Selin Gulmus Kolay
Phone: +90 312 219 62 19
Email: selin@h2otherapeutics.com
Date Prepared: November 15th, 2022

2. **Device:**

Trade Name: Parky App
Common Name: Movement Disorder Monitoring System
Classification Name: Tremor Transducer (21 CFR 882.1950)
Device Classification: II
Product Code(s): GYD, NXQ, ISD

3. **Predicate Device**

K213519, Rune Labs Kinematics System. The predicate device has not been recalled.

4. **Device Description**

Parky App is a symptom tracker mobile app for Parkinson's Disease patients. It collects motion data through Apple Watch continuously and quantifies tremor and dyskinesia episodes based on clinically validated MM4PD algorithm. Tracked symptoms are reported as daily, weekly and monthly. Each report is shared with the prescribing healthcare professional through email. The mobile app has a medication reminder module which the patients can manually enter their medication schedule, receive on-time reminder notifications on Apple Watch and iPhone and can respond to them as "taken" or "not yet taken". Parky also reports daily step counts provided by Apple Services - HealthKit. Figure 1 provides a schematic demonstration of the system components and device operation.

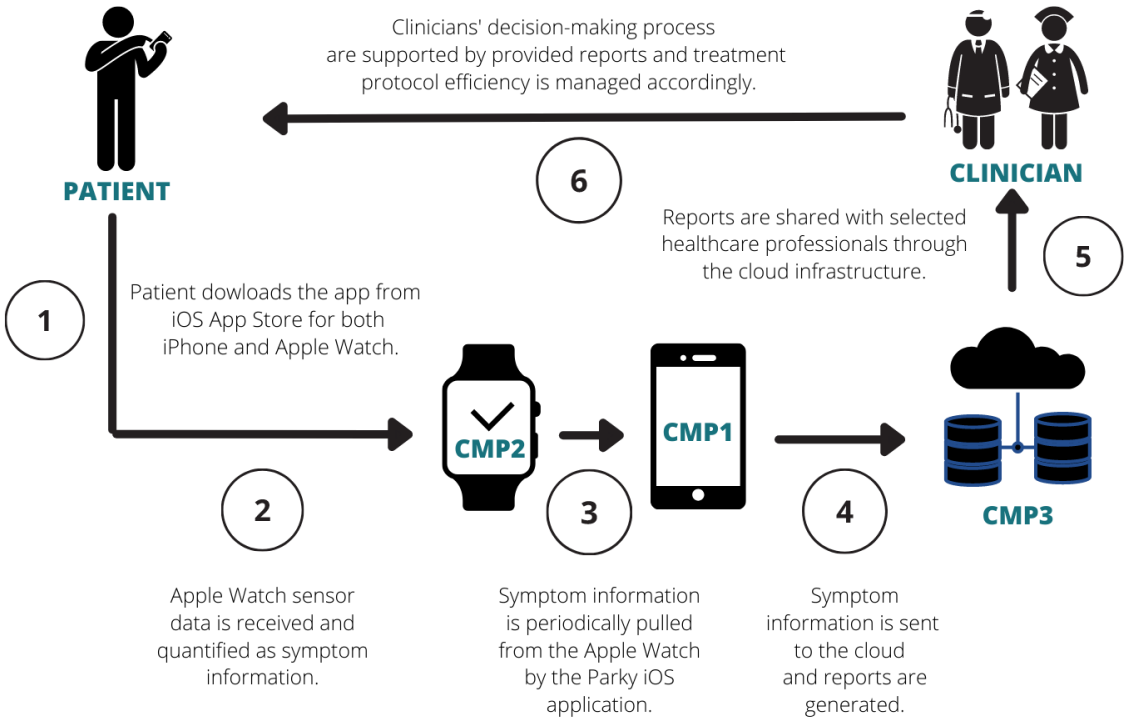


Fig.1 System Components and Operation Overview

5. Indications for Use

The Parky App is intended to quantify kinematics of movement disorder symptoms including tremor and dyskinesia, in adults (45 years of age or older) with mild to moderate Parkinson's disease.

6. Comparison of Technological Characteristics to The Predicate

The proposed device, Parky App has identical working principle to the predicate, K213519, Rune Labs Kinematics System. Both devices collect movement recordings by the help of Apple Watch motion sensor and quantified Parkinson's Related movement disorders, specifically tremor and dyskinesia. Table 1 below provides a technological comparison of the proposed and predicate devices:

Table 1: Comparison of Parky App to Predicate Device.

Characteristic	Proposed Device	Predicate, K213519	Comparison
Intended Use	To measure the degree of tremor caused by certain diseases.	To measure the degree of tremor caused by certain diseases.	Identical to the predicate device.
Indications for Use	The Parky App is intended to quantify kinematics of movement disorder symptoms including tremor and dyskinesia, in adults (45 years of age or older) with mild to moderate Parkinson's disease.	The Rune Labs Kinematic System is intended to quantify kinematics of movement disorder symptoms including tremor and dyskinesia, in adults (45 years of age or older) with mild to moderate Parkinson's disease.	Identical to the predicate device.
Rx vs OTC	Rx	Rx	Identical to the predicate device.
Measurement Method	Recording of symptoms via wrist worn watch.	Recording of symptoms via wrist worn watch.	Identical to the predicate device.
Biocompatibility	Apple watch is manufactured from non-skin irritating and non-sensitizing materials.	Apple watch is manufactured from non-skin irritating and non-sensitizing materials.	Identical to the predicate device.
Electrical Safety	Electrical safety was assessed according to IEC 62368-1 (2014), "Audio/video, information and communication technology equipment – Part 1: Safety requirements."	Electrical safety was assessed according to IEC 62368-1 (2014), "Audio/video, information and communication technology equipment – Part 1: Safety requirements."	Identical to the predicate device.
Electromagnetic Compatibility (EMC)	The Apple Watch conforms to EU standards EN 301	The Apple Watch conforms to EU standards EN 301	Identical to the predicate device.

Characteristic	Proposed Device	Predicate, K213519	Comparison
	489-1 (V2.2.20), EN 301 489-3 (V2.1.1), EN 301 489-17 (V3.2.0), and EN 301 489-52 (V1.1.0).	489-1 (V2.2.20), EN 301 489-3 (V2.1.1), EN 301 489-17 (V3.2.0), and EN 301 489-52 (V1.1.0).	
Software	Software Validation was conducted per FDA Guidance "Content of Premarket Submissions for Device Software Functions" issued on May 11, 2005	Software testing established that the system meets the software requirements and user needs for the intended uses.	Identical to the predicate device.
Cybersecurity	Cybersecurity threat analysis and mitigation has been conducted according to "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices".	Not specified.	We have conducted extensive cybersecurity testing and mitigation efforts to ensure the security of our patient data.
Outputs and Features	The Rune Lab device outputs are the percentage of the time that tremor and dyskinesia were likely to occur.	The Rune Lab device outputs are the percentage of the time that tremor and dyskinesia were likely to occur.	Identical to the predicate device.
Data Transmission	Cellular or Wireless Network	Cellular and Wireless Network	Identical to the predicate device.
Over-the-Counter Software	Utilizes Apple's MM4PD API and Apple Watch's accelerometer to measure and quantify dyskinesia and tremor related to Parkinson's Disease	Utilizes Apple's MM4PD API and Apple Watch's accelerometer to measure and quantify dyskinesia and tremor	Identical to the predicate device.

Characteristic	Proposed Device	Predicate, K213519	Comparison
		related to Parkinson's Disease	
Performance Data	Device Measurements highly correlated to clinical evaluations of tremor severity (Rank Correlation Coefficient=0.80) and mapped to expert ratings of dyskinesia presence (P<0.001) during in-clinic tasks. Device captured symptom changes in response to treatment that matched the clinician's expectations in 94% of evaluated subjects.	Rune medical uses the same API that was validated with the same performance data, published by Powers et al [1].	Identical to the predicate device.

In summary, Parky App uses the same underlying software (MM4PD) and hardware (Apple Watch) towards its intended use as the predicate device. Software validation and cybersecurity assessment have been conducted to ensure the safe and effective use of the app, and to safeguard the collected data. The proposed device is substantially equivalent to the predicate towards its intended use.

The medication reminder, product code NXQ, and the step counter, ISD, are both 510(k) exempt devices and are not subject to 510(k) notification.

7. Safety

7.1. EMC and Electrical Safety

Parky App uses the same generation of apple watch as the predicate device. Apple Watch conforms to the following EMC and Electrical Standards:

[1] Powers R, Etezadi-Amoli M, Arnold EM, Kianian S, Mance I, Gibiansky M, Trietsch D, Alvarado AS, Kretlow JD, Herrington TM, Brillman S, Huang N, Lin PT, Pham HA, Ullal AV. Smartwatch inertial sensors continuously monitor real-world motor fluctuations in Parkinson's disease. Sci Transl Med. 2021 Feb 3;13(579):eabd7865. doi: 10.1126/scitranslmed.abd7865. PMID: 33536284.

- Electrical safety was assessed according to IEC 62368-1 (2014), “Audio/video, information and communication technology equipment – Part 1: Safety requirements.”
- Apple Watch conforms to EU standards EN 301 489-1 (V2.2.20), EN 301 489-3 (V2.1.1), EN 301 489-17 (V3.2.0), and EN 301 489-52 (V1.1.0).

7.2. Biocompatibility and Sterility

Parky App uses the same generation of Apple Watch as the predicate device. All patient contacting materials are identical to the predicate device. The proposed device is not intended to be used as sterile.

8. Software

8.1. Software Validation and Verification

Software documentation was provided according to the FDA guidance titled: “Content of Premarket Submissions for Device Software Functions”, issued on May 11, 2005. The level of concern was moderate as defined in the guidance.

8.2. Cybersecurity

Parky is an internet-connected app. Thus, a Cybersecurity Threat Assessment and Remediation Analysis (CTARA) was conducted, and all risks were mitigated per the FDA guidance titled: “Content of Premarket Submissions for Management of Cybersecurity in Medical Devices” issued on October 18, 2018.

9. Performance Data

9.1. Clinical Testing

A clinical study[2] with 343 participants with PD, including a longitudinal study of up to 6 months in a 225-subject cohort was conducted to demonstrate the ability of the MM4PD API used in Parky App to continuously track and categorize two common symptoms of Parkinson’s disease: Tremor and Dyskinesia. M4PD measurements correlated to clinical evaluations of tremor severity (Rank Correlation Coefficient=0.80) and mapped to expert ratings of dyskinesia presence ($P<0.001$) during in-clinic tasks. The ability of MM4PD to identify tremors and the likelihood of dyskinesia was tested with the final algorithm in holdout sets. In addition, MM4PD captured symptom changes in response to treatment that matched

[2] Powers R, Etezadi-Amoli M, Arnold EM, Kianian S, Mance I, Gibiansky M, Trietsch D, Alvarado AS, Kretlow JD, Herrington TM, Brillman S, Huang N, Lin PT, Pham HA, Ullal AV. Smartwatch inertial sensors continuously monitor real-world motor fluctuations in Parkinson's disease. Sci Transl Med. 2021 Feb 3;13(579):eabd7865. doi: 10.1126/scitranslmed.abd7865. PMID: 33536284.

the clinician's expectations in 94% for cases of full patient history and 87,5% for cases of blind classification with 3 expert raters. There were no serious adverse events associated with the use of the device.

Table S1 below summarizes the patient demographics across all studies reported by Powers et al., 2021.

Table S1. Study demographics. Patient demographics across all studies

	Pilot study **PD patients in-clinic + 1 week live-on**	**Longitudinal patient study** **PD patients long-term live-on**	**Longitudinal control study** **Elderly controls**
Age [± Standard Dev]	68.1 yrs [±9.0]	71.4 yrs [±8.9]	74.7 yrs [±5.4]
Years with PD [± Standard Dev]	6.5 yrs [±5.6]	10.3 yrs [±6.5]	n/a
Gender	36 Female, 82 Male	69 Female, 156 Male	85 Female, 85 Male, 1 unknown
Most Affected Side	62 Right / 39 Left / 17 unspecified	105 Right / 120 Left	n/a
History of Tremor	-	166/225 Participants	n/a
History of Dyskinesia (History of Chorea)	-	94/225 Participants (66/94 with dyskinesia)	n/a
History of Freezing Gait	-	85/225 Participants	n/a
History of Slow Gait	-	172/225 Participants	n/a
		*self-reported history	

An overview of the study design is provided below in Figure S1. This figure lists the design and validation phases with their respective number of subjects from each group.

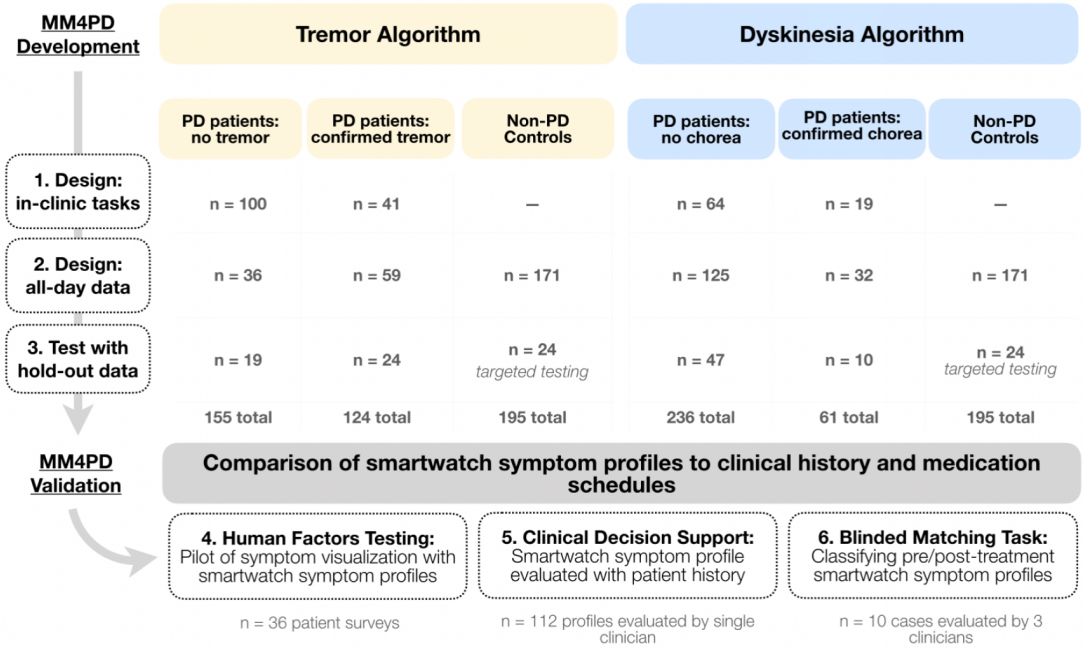


Fig. S1. Overview of data collected for MM4PD development and validation. MM4PD development of tremor and dyskinesia algorithms used sensor data from both in-clinic tasks and all-day data in Parkinson's patients as well as several elderly, control subjects with no reported Parkinson's disease. Some patients provided in-clinic data with both tremor and no tremor across different sessions. The algorithm was tested with a hold-out dataset that had all-day data and a single in-clinic visit from a subset of subjects in the longitudinal patient study. MM4PD outputs were further validated in 3 ways: i) a human factors pilot to ensure patients understood the smartwatch symptom profiles, ii) a comprehensive review to determine where smartwatch symptom profiles matched clinician expectations when used alongside a comprehensive patient history, and iii) a blinded matching task by 3 expert raters who classified smartwatch symptom profiles as pre or post-treatment for a given medication change.

As described in Fig S1. above and detailed in Table 1 below, to design and validate MM4PD, 9 study results are presented within the Clinical Trial Report (Powers et al., 2021):

1a	Tremor algorithm design with in-clinic tasks	**1b**	Dyskinesia algorithm design with in-clinic tasks
2a	Tremor algorithm design with all-day data	**2b**	Dyskinesia algorithm design with all-day data
	Design lock for MM4PD Tremor and Dyskinesia Algorithms: minute-by-minute measurements ready to be tested in real-world continuous use to match MDS-UPDRS tremor constancy		
3a	Tremor algorithm test with hold-out data during the longitudinal patient study	**3b**	Dyskinesia algorithm test with hold-out data during the longitudinal patient study
	Patient symptom profiles generated based on 15 min averages of MM4PD minute-by-minute outputs		
4	Human factors testing for symptom profiles through patient surveys		
5	Evaluation of symptom profiles by a clinician with access to patient history		
6	Evaluation of symptom profiles by 3 blind clinicians without access to patient history		

Table 1. Description of Design and Validation Studies Out of all 9 study results listed above, 3a and 3b were used to validate the tremor and dyskinesia algorithm performance in hold-out data sets and out-of-clinic settings, respectively. (Please see Fig 3E and 4E). 5 and 6 validate that the patient symptom profiles (generated through 15 minutes averages of MM4PD minute-by-minute outputs for tremor and dyskinesia separately) match clinician expectations based on MDS-UPDRS constants either with or without access to patient history, respectively (Please see Fig 6)

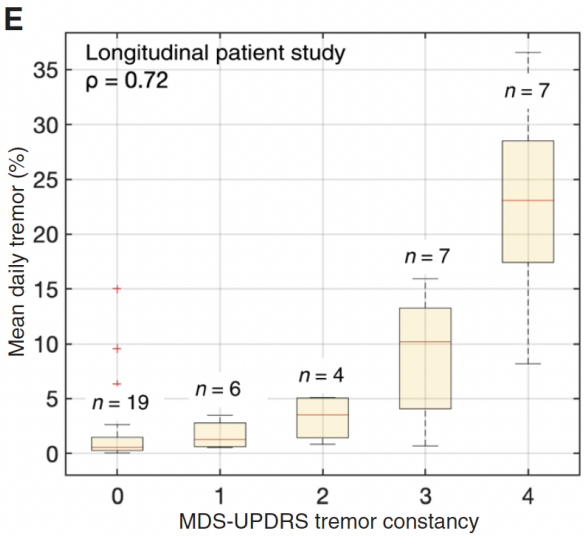


Fig. 3E. Smartwatch estimates of tremor severity and presence correlate to MDS-UPDRS ratings Mean daily smartwatch tremor estimates correlated with MDS-UPDRS tremor constancy ratings from the subject's last in-clinic visit in hold-out (n = 43) set with a Spearman's rank correlation of 0.72.

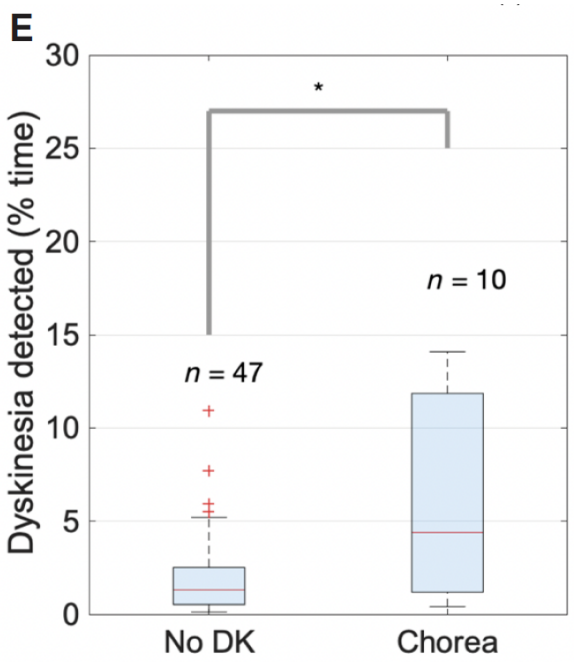
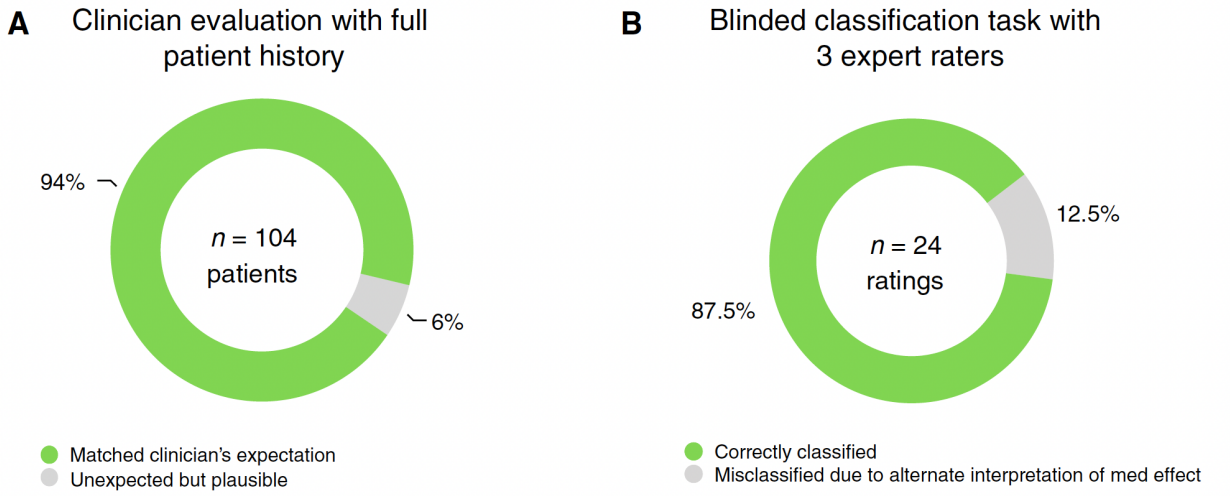


Fig. 4E. Smartwatch choreiform dyskinesia detection matches clinical evaluation. In a hold-out dataset (n=57) from the longitudinal patient study, the percentage of time dyskinesias were detected for the chorea group (5.9 ± 5.3%) significantly differed from subjects with no reported dyskinesias (2.0 ± 2.2%) (P = 0.027, Wilcoxon rank sum test)



Clinician evaluation in longitudinal patient study	*n*
Patients with sufficient data who underwent medication or DBS changes	112
Symptom data inconclusive (excluded)	(8)
Symptom data changes matched medication change	98
Symptom data unexpected but plausible	6
Total assessed	104

Pre/post-treatment smartwatch symptom profile classification	*n*
Ratings from *n* = 10 tasks and 3 raters	30
Insufficient or inconclusive signal (excluded)	(6)
Classified correctly	21
Misclassified (rater choice confounded by plausible, alternate medication effect)	3
Total assessed	24

Fig. 6. Smartwatch symptom profiles match clinician expectations and provide quantitative evidence for cases with uncertainty. The clinician reviewed the smartwatch symptom profiles of 112 subjects in the longitudinal patient study who underwent treatment changes. (A) Symptom changes matched the clinician's expectation of the prescribed medication change in 94% of cases. Unexpected cases revealed plausible incidence of known side effects to medications. (B) Three blinded movement disorder specialists classified 10 sets of profiles as pre-or post-treatment using only the patient's medication schedule and MDS-UPDRS tremor and dyskinesia ratings from the intake visit; 87.5% of classifications were correct; three misclassifications occurred because raters presumed that an alternate medication had a dominant effect. Six cases were deemed inconclusive and were excluded.

In summary, MM4PD algorithm outputs significantly correlate with MDS-UPDRS scores of the patients. In addition, system profiles generated through 15-minute means of MM4PD outputs match clinician expectations in out-of-clinic settings.