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Letter to the Editor

Remote Administration of the MDS-UPDRS in the Time of COVID-19 and Beyond

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The COVID-19 pandemic has disrupted clinical research. Recognizing the importance of participant and research personnel safety, funding and regulatory agencies have issued guidance encouraging temporary modifications to research studies including a shift to remote assessments [1–3]. In the midst of the COVID-19 pandemic, the appeal of conducting remote research visits for individuals with Parkinson's disease (PD) is clear.

Operations for virtual PD research studies [4, 5], have been able to continue seamlessly. In contrast, in-person research studies have had to contend with missed or incomplete visits. In this personal viewpoint, we offer our perspective on remote Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) motor assessment [6], for those considering or in the process of transitioning to remote video-based visits.

The feasibility of conducting a modified version of the MDS-UPDRS motor, without assessment of rigidity or postural stability, has been previously demonstrated [8–10]; however, it has not been adequately validated against in-person assessment. A secondary analysis of clinical trial data (CALM-PD), which compared a modified Unified Parkinson Disease Rating Scale (UPDRS) motor to the standard UPDRS motor, concluded that the modified version would be cross-sectionally and longitudinally reliable [11]. Direct comparison of in-home, video-based versus in-person administration of the modified UPDRS motor demonstrated moderate overall agreement [8]. In a small study that compared in-person and video-based modified MDS-UPDRS motor assessment, median difference in scores was 3.0 (IQR 1.5–9.0) [12]. Of concern, lower extremity tremor could not be assessed in 10/11 participants. In a recently completed study embedded within a phase 3 clinical trial, 38 participants underwent remote assessment within 4 weeks of in-person assessment [13]. The correlation between the remote and in-person MDS-UPDRS motor was moderate (ICC = 0.51), with lower correlations likely driven by completion by different examiners. Critically, no means for direct comparison of remote and in-person MDS-UDPRS motor scores exists, making interpretation of longitudinal data problematic [7]. The inability to assess rigidity

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and postural instability impedes such direct comparison and complete phenotypic characterization. Efforts are underway to validate the modified MDS-UPDRS motor [4].

Collectively, the authors have conducted hundreds of remote MDS-UPDRS motor assessments of individuals at-risk for and with PD of different stages of disease. We can confidently speak to the feasibility and safety of conducting remote assessments. We take precautions to minimize the risk of falls, including requesting participants walk with their assistive device (when applicable) and deferring gait assessment when prudent. We collect the participant's location at the time of the visit in case of emergency. Over two years, we conducted over 550 remote visits with PD participants across three separate research studies [4, 5, 14]. We had one fall, which occurred outside administration of the MDS-UPDRS in a participant who experienced falls on a daily basis and have never contacted emergency services. Excluding rigidity and postural instability items, we have been able to rate 98.3% (15,179/15,444) of items with assessment of toe tapping, lower extremity rest tremor, and leg agility most commonly missed. Remote MDS-UPDRS assessment is safe and feasible.

However, several factors can affect the accuracy of remote assessment. Environmental factors (lighting, background, space) can reduce or prohibit assessment of certain elements. With in-person visits, examiners can easily visualize the entire body throughout the visit, which enables accurate assessment of global bradykinesia and rest tremor. To achieve this during a remote visit, the camera should be approximately 6–8 feet from the participant. However, this is often not possible. Moreover, evaluation at this distance may impede assessment of hypomimia, postural tremor and action tremor. Repositioning of the camera and participant should be anticipated. In our opinion, remote MDS-UPDRS assessment likely underrates global bradykinesia and rest tremor. Additionally, space may not allow for adequate assessment of gait and freezing of gait. Technical factors (internet speed, quality of connection and camera) can similarly limit assessment. Laptops, tablets, and smartphones can be easily repositioned whereas the inability to maneuver desktop cameras may impede assessment of lower extremities. Subtle bradykinesia or tremor can be difficult to appreciate remotely, even under ideal conditions. A poor connection can make assessment more challenging, but may be helped by closer proximity to the internet router.

Participant factors (age, access/familiarity with technology, disease stage, cognitive status) can present additional challenges. In our experience, remote visits can be successfully conducted among older individuals and those with substantial disability [15] and may be even more valuable among this group given their travel-related challenges and higher risk for worse outcomes with COVID-19 [16]. To improve participant comfort and the likelihood of success, adequate preparation is critical. In test visits, coordinators can explain how to connect, determine the ideal set-up, and review the evaluations. The inclusion of care partners in visits can also help mitigate some of these issues and their participation should be encouraged for participants with more advanced disease. Lastly, investigator factors (familiarity with the technology and with remote examination) can impact assessment. Investigators, even those well-experienced, should be trained on remote assessment by viewing sample recordings of remote MDS-UPDRS examinations and shadowing a live visit. To assist researchers, we have made the protocol and model consent form for one of our virtual studies (AT-HOME PD) freely available (https://www.athomepd.org/professionals).

Clinical researchers must find a way to safely continue important research during the COVID-19 pandemic. While remote MDS-UPDRS motor assessment presents some challenges, many of these can be mitigated, and in our opinion, remote assessment is appropriate for many on-going research studies. However, the specifics of the research should guide this decision; we would not recommend remote MDS-UPDRS motor assessment for a treatment trial in which it is the primary outcome measure. One viable alternative is the remote assessment of patient-reported outcomes. Digital tools, such as wearable sensors, which can provide objective, real-world data have enormous potential as surrogate outcome measures and may ultimately supplant remote MDS-UPDRS assessment. More work is needed to validate remote MDS-UPDRS motor assessment; however, we anticipate that one long-term effect of the COVID-19 pandemic will be that more researchers will embrace the use of video-based visits and digital tools.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to report.

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Earl R. Dorsey is employed by the University of Rochester and has ownership Interests in Grand Rounds, an online second opinion service. He has consulted for 23 and Me, Abbott, Abbvie, Amwell, Biogen, Clintrex, CuraSen, DeciBio, Denali Therapeutics, GlaxoSmithKline, Grand Rounds, Huntington Study Group, Informa Pharma Consulting, medical-legal services, Mednick Associates, Medopad, Olson Research Group, Origent Data Sciences, Inc., Pear Therapeutics, Prilenia, Roche, Sanofi, Shire, Spark Therapeutics, Sunovion Pharmaceuticals, Voyager Therapeutics, and ZS Consulting. He has received honoraria from Alzheimer's Drug Discovery Foundation, American Academy of Neurology, American Neurological Association, California Pacific Medical Center, Excellus BlueCross BlueShield, Food and Drug Administration, MCM Education, Michael J. Fox Foundation, Stanford University, UC Irivine, and University of Michigan. He has received grants and research support from Abbvie, Acadia Pharmaceuticals, AMC Health, BioSensics, Burroughs Wellcome Fund, Greater Rochester Health Foundation, Huntington Study Group, Michael J. Fox Foundation, National Institutes of Health, Nuredis, Inc., Patient-Centered Outcomes Research Institute, Pfizer, Photopharmics, Roche, and Safra Foundation.

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