The goals of this subgroup are to: 1) recommend Best Practices for choice of digital health outcome measures and 2) present Guidance for digital data sharing for clinical trials on PD. Digital health outcomes include measures derived from technology that is attached to the moving participant to detect clinical signs (e.g., bradykinesia, tremor, gait and balance disorders, blood pressure, heart rate variability, etc.) or detects health behaviors in an environment (e.g., sleep, activity, cognitive function). Digital Health Outcomes for these practices and guidance do not include electronically-collected patient reported outcomes about self-perceived feelings, observations, judgements (e.g., quality of life, medication or sleep diaries or clinical rating scales, etc.). However, the guidance also includes use of phones, tablets, computers or any other technically-validated devices that accurately measure how people move, behave, think, etc. although recommendations for measuring outcomes are device-agnostic.

Each member of the subgroup took turns adding to the draft of recommendations started by the Chairperson. Early, the subgroup decided not to recommend specific digital health outcomes because the field is too new and dynamically changing. They also decided to make recommendations device-agnostic because technology is changing so quickly, any specific recommendations will quickly become out of date. Instead, they focused on statistical criteria that investigators should weigh to select digital outcomes (depending upon the goals of their study) and on how to select the appropriate technology to measure their outcomes. For example, investigators should select measures that have technical validation, relate to patient quality of life judgement, are reliable, sensitive to change, related to clinician’s judgement, etc., as well as patient burden and feasibility. They also made a summary of “lessons learned” about what is now understood about digital health data. For example, the most accurate measures of stride length come from inertial sensors on the feet, not the wrist or lumbar area and although tremor measurement can be technically valid (accurate), it may not be well related to what patients with PD care most about.

The subgroup recommends that investigators consider the disease stage in picking outcomes, because some digital outcomes are more appropriate for early-stage versus late-stage disease. For example, arm swing range of motion is very sensitive sign of progression during early, but not late, disease stages and gait quality cannot be measured reliably when patients need to use assistive devices in later disease stages.

<table>
<thead>
<tr>
<th>Summary of Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guidance Document</td>
</tr>
<tr>
<td>Best Practices for Digital Health Outcomes</td>
</tr>
<tr>
<td>Guidance for Digital Data Sharing</td>
</tr>
</tbody>
</table>

Best Practices for Digital Health Outcomes
- At this time, all digital health outcomes for PD clinical intervention trials are generally considered EXPLORATORY because technologies are changing and improving rapidly without consensus on specific hardware or software for PD.
Decisions on which specific Digital Health Outcomes to select should depend upon achieving the best statistical criteria, including meaningfulness to patients [Minimal Clinically Important Difference (MCID)], technical verification, sensitivity/specificity to cohort, clinical validity, sensitivity to change [Minimal Detectable Change (MDC)], effect size, reliability, etc.

Clinical validation of outcomes depends on context of use (setting, active versus passive, particular patient population, etc.)

Most of the current evidence for Digital Health Outcomes for PD use body-worn sensors during prescribed tasks (e.g., rapid alternating arm rotations for bradykinesia, gait, etc.) but many studies are using passive monitoring during normal daily activities.

Recommended Digital Health Outcomes for PD at the current time include gait, balance, bradykinesia and tremor for in-clinic, prescribed tasks.

Emerging Digital Health Outcomes for PD in need of further development include motor fluctuations, freezing of gait, sleep, cognition, and speech.

Reporting of Digital Health Outcomes should use the EVIDENCE (EValuating connecteD sENsor teChnologIEs) checklist that was developed by a multidisciplinary group of content experts from the Digital Medicine Society.

Guidance for Digital Data Sharing are brief, as they rely upon other NIH, The Institute of Electrical and Electronics Engineers (IEEE), dHealth data repository standards (which are listed as resources). In general, digital health data sharing should include information about: 1) Subject demographics, 2) Parkinson’s disease, 2) Technology, and 3) Environment/Context. Raw data, as well calculated outcomes, should be uploaded to the server, if possible. Contact information of investigators should be included.

Since so many digital health measures could be altered by dopamine replacement therapy, it is important for investigators to specify whether measures of digital health were taken when patients were in the practical On or practical Off state, and ideally the time of their last levodopa dose prior to measurement. Environmental context may affect digital health outcome measures, such as walking between narrow spaces, which could trigger freezing of gait not apparent in wider spaces.

Unmet needs; unanswered questions:

1. Some domains of digital health, such as gait characteristics in people with PD, have much more evidence in the literature than other domains, such as sleep quality at home or cognitive performance in daily life activities. Thus, a committee focused specifically on summarizing evidence for the best digital mobility (gait, turning, balance, postural transitions) measures for PD could likely make more specific mobility outcome recommendations (working with the Michael J Fox foundation committee on digital gait).
2. Differences between the same digital health outcomes when collected during prescribed tasks (in clinic/lab or home) versus passively, during daily life (such as during a short walk in the clinic versus a week of monitoring natural gait at home) are not fully understood.
3. The accuracy of measuring REM sleep disorder in the home is undeveloped.
4. The accuracy of detecting falls with body-worn sensors is unsatisfactory.
5. More accurate measures of motor fluctuations during daily life are needed.
6. Cognitive outcomes measured passively, during daily life activities, such as typing speed/accuracy, could be useful.