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## **Quantitative mobility metrics from a wearable sensor predict incident parkinsonism in older adults**

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## **Abstract**

**Introduction:** Mobility metrics derived from wearable sensor recordings are associated with parkinsonism in older adults. We examined if these metrics predict incident parkinsonism.

**Methods:** Parkinsonism was assessed annually in 683 ambulatory, community-dwelling older adults without parkinsonism at baseline. Four parkinsonian signs were derived from a modified Unified Parkinson's Disease Rating Scale (UPDRS). Parkinsonism was based on the presence of 2 or more signs. Participants wore a sensor on their back while performing a 32 foot walk, standing posture, and Timed Up and Go (TUG) tasks. 12 mobility scores were extracted. Cox proportional hazards models with backward elimination were used to identify combinations of mobility scores independently associated with incident parkinsonism.

**Results:** During follow-up of 2.5 years (SD=1.28), 139 individuals developed parkinsonism (20.4%). In separate models, 6 of 12 mobility scores were individually associated with incident parkinsonism, including: Speed and Regularity (from 32 ft walk), Sway (from standing posture), and 3 scores from TUG subtasks (Posterior sit to stand transition, Range stand to sit transition, and Yaw, a measure of turning efficiency). When all mobility scores were analyzed together in a single model, 2 TUG subtask scores, Range from stand to sit transition (HR, 1.42, 95%CI, 1.09, 1.82) and Yaw from turning (HR, 0.56, 95%CI, 0.42, 0.73) were independently associated with incident parkinsonism. These results were unchanged when controlling for chronic health covariates.

**Conclusion:** Mobility metrics derived from a wearable sensor complement conventional gait testing and have potential to enhance risk stratification of older adults who may develop parkinsonism.

#### **Keywords**

parkinsonism; gait testing; biosensor; accelerometry; longitudinal

## **INTRODUCTION**

Parkinsonism, including bradykinesia, tremor, rigidity and gait impairment, is common in older adults without Parkinson disease (PD) and as it increases with age it may affect 50% or more of the population by age 85.[1] Parkinsonism is a heterogeneous syndrome, which is not limited to PD, but can be caused by diverse etiologies, some of which are amenable to treatment.[2] Furthermore, parkinsonism is associated with adverse health outcomes including death, disability, and cognitive impairment.[3] Given the magnitude and consequence of parkinsonism in our aging population, identification of at-risk individuals offers the potential for early interventions that which may prevent the development of parkinsonism.[4]

Conventional mobility metrics, such as gait speed, are sensitive but non-specific predictors of parkinsonism.[5, 6] Mobility is a multi-dimensional trait derived from dissociable neural control systems within the central nervous system.[7, 8] Investigations in gait laboratories have quantified additional facets of mobility necessary for successful locomotion.[9, 10]

Emerging technologies including wearable sensors show promise for extending these advances beyond the lab or hospital setting to varied venues including outpatient clinics and community studies of aging.[11, 12]

In a prior cross-sectional study, we found that sensor-derived mobility metrics were related to the severity of parkinsonian signs in older adults. [13–15] However, it is not known if these sensor-derived mobility metrics are associated with incident parkinsonism. To address this question, we used clinical data from older adults, participating in two community-based longitudinal cohort studies, who undergo annual motor testing for parkinsonian signs, as well as mobility testing with a wearable sensor.

## **METHODS**

#### **Participants**

Participants were from two ongoing longitudinal cohort studies, recruited from retirement communities and subsidized housing facilities in the Chicago metropolitan area, the Rush Memory and Aging Project (MAP) and the Minority Aging Research Study (MARS). [16, 17]

All procedures in both studies were approved by the Institutional Review Board of Rush University Medical Center and were conducted in compliance with the Declaration of Helsinki. Written informed consent was obtained from all study participants.

There were 815 participants (MAP: N=619; MARS: N=196) who did not have clinical parkinsonism at their first visit with instrumented gait testing, which served as baseline visit for this study. Since these analyses focused on the association of mobility metrics with incident parkinsonism, we excluded participants who did not have a follow-up assessment (n=132), because they either died before the second assessment or had not yet reached their first follow-up visit. The characteristics of the remaining 683 individuals at their baseline visit (MAP: N=500; MARS: N=183) are summarized in Table 1.

#### **Demographics and Other Chronic Health Covariates**

Demographics covariates were obtained at study entry (Table 1). Chronic health conditions included the number out of 3 vascular risk factors (diabetes, hypertension, smoking [median=0; Q1,0, Q3,3]) and the number out of 4 vascular diseases (claudication, congestive heart failure, myocardial infarction, stroke [median=0; Q1,1, Q3,4]). BMI was calculated from measured height and weight.

#### **Assessment and Categorization of Individuals with Parkinsonism and PD**

**Global Parkinsonism Score:** The annual evaluation includes a modified version of the Unified Parkinson's Disease Rating Scale (UPDRS) [18] administered by trained nurse clinicians.[19] 26 items which assess 4 parkinsonian signs (parkinsonian gait, bradykinesia, rigidity, and tremor, including rest tremor and action tremor) were summarized as continuous global parkinsonism score, as previously described.[19] This global parkinsonism score allows for the assessment of the severity of parkinsonian signs in all

individuals, including those with mild signs not meeting criteria for parkinsonism (described below).

**Categorization of Parkinsonism:** Previously validated categories of parkinsonism were based on the number of parkinsonian signs present. A sign was present if 2 or more of their respective items had at least a score of 1 indicating mild abnormality. *Parkinsonism* was present if 2 or more signs were documented. Possible parkinsonism was present if there was 1 sign, and No parkinsonism if there were none.[3] Prior publications have established interrater reliability between nurse clinicians and a movement disorder specialist for both the global parkinsonism score and categorization of parkinsonism.[3, 19]

**Diagnosis of PD:** A diagnosis of PD was based on the self-reported history of PD for which the participant was treated by a physician with levodopa or other dopamine agonists. [20]

#### **Assessment of Mobility**

**Wearable Sensor:** Mobility testing with a wearable sensor (Dynaport MT, McRoberts B.V., The Netherlands) positioned on the lower back with a neoprene belt was performed at the participant's residence. This device consists of three orthogonally oriented piezoelectric accelerometers and three gyroscopic sensors for 100 Hz sampling of three-dimensional acceleration and rotation rate of the lower trunk.

**Mobility Performances:** Three performances were recorded. A) 32 ft walk: Participants walked at their self-selected speed on a marked 8 ft course back and forth twice without stopping. The length of the course was limited to 8 ft, in order to ensure that the task could be performed in participants' homes.[15] B) Modified TUG: Participants were instructed to stand up from a chair, walk 8 ft at a comfortable self-selected speed, turn and walk back to the chair and sit down again. C) Standing Posture: Participants were asked to stand for 20 seconds in a comfortable position with their eyes closed.

**Extraction of Mobility Measures:** All three performances were recorded in a single file, with markers embedded in the file to identify the beginning and the end of each performance. Before automated processing of the segmented files, a research assistant confirmed correct marker locations in the segmented performances, using a custom Matlabbased graphical user interface. The single file is then segmented into separate files for each performance tested, based on the embedded markers.

Mobility measures were extracted from each of the performances using previously described formulas [21–23]. The TUG is composed of 4 different movements or subtasks.[21, 22] This study examined 3 TUG subtasks including: 1) transition from sit to stand  $(S1)$ , 2) transition from stand to sit (S2), and 3) turning subtasks and did not include the walk components. The TUG walk subtasks were not included so as not to duplicate the walk measures obtained from the 32ft walk.

**Mobility Scores:** In a previous study we used available literature and principal component analyses to guide our construction of 12 mobility scores, which summarize the 26 measures

extracted from the 5 mobility subtasks.[15] Table 2 shows the relationship between the mobility subtasks, measures and scores. Each mobility score had a standard deviation equal to 1, and higher values corresponded to more movement. These 12 mobility scores were used in the analyses described below.

#### **Statistical Analysis**

The goal of this multi-stage analysis is to identify a group of mobility scores independently associated with incident parkinsonism. Stage 1 determined which of the scores were individually associated with incident parkinsonism by examining each of the 12 scores in a separate Cox proportional hazards model. *Stage 2* determined which scores from each of the five mobility subtasks were independently associated with incident parkinsonism. We included all mobility scores of the respective subtask together in a single Cox proportional hazards model and employed backward elimination. To ensure that we did not exclude a potential significant association in this stage, we chose p<0.1 as cutoff to carry forward mobility scores to Stage 3. Stages 1 and 3 employed a conventional nominal significance of p<0.05. The Stage 2 analysis cannot be performed for the Sway mobility score, as there is only one mobility score summarizing the standing posture subtask. Stage 3 determined which mobility scores from all 5 subtasks were independently associated with incident parkinsonism when analyzed together in a Cox proportional hazards model with backward elimination with the Sway score and all mobility scores which survived Stage 2 for the other four subtasks.

The same 3-stage approach was used to determine which mobility scores independently predicted incident possible parkinsonism, in persons with no parkinsonian signs at baseline. In order to be able to compare across subtasks, the demographic variables (age, sex, education and race) were included in all models and only the mobility scores varied with backward elimination.

In further analyses, we examined if the addition of terms for chronic health conditions or a term for the clinical severity of parkinsonism at baseline, which are known to predict parkinsonism, attenuated the association of the final combinations of mobility scores from Stage 3 with incident parkinsonism. We then employed c-statistics to evaluate the value added of these different terms for predicting incident parkinsonism.[24] A higher c-statistic suggests a better predictive model. Models were examined graphically and analytically and assumptions were judged to be adequately met. Programming was done in SAS version 9.3 (SAS Institute Inc., Cary, NC).

#### **RESULTS**

We included 683 participants in our longitudinal analysis. Clinical characteristics at baseline are summarized in Table 1 and the individual mobility measures in Table 2.

#### **Association of sensor-derived mobility scores with incident parkinsonism**

During an average 2.5 years of follow-up (SD=1.3, range 1 to 6 years), 139 out of 683 (20.4%) participants developed parkinsonism. In Stage 1 we found that six out of 12 mobility scores were associated with incident parkinsonism (Table 3, Stage 1).

Stage 2 examined combinations of mobility scores within each of the 4 mobility subtasks that were summarized by 2 or more mobility scores. Following stepwise backward elimination, 5 mobility scores remained associated with incident parkinsonism (Table 3, Stage 2).

In Stage 3, we included the independently associated mobility scores for all 5 mobility subtasks (5 mobility scores which remained significant after Stage 2, plus Sway) in a single model, to determine which mobility scores were independently associated with incident parkinsonism. Two mobility scores (which did not include gait speed) remained associated with incident parkinsonism: Range from TUG stand to sit (S2) transition, and Yaw (as a measure of turning efficiency) from TUG turning (Table 3, Stage 3). These results were unchanged when we excluded 4 individuals with a clinical diagnosis of PD (data not shown).

Chronic health conditions can contribute to parkinsonian signs in older adults.[25] We therefore repeated the final model including the two mobility scores and added terms to control for BMI, four chronic vascular diseases and three vascular risk factors. TUG stand to sit Range and TUG turning Yaw mobility scores remained associated with incident parkinsonism (Table e1, Model 2).

To show that the sensor-derived mobility scores add to the previously established association of a global parkinsonian score with incident parkinsonism [25], we repeated the previous model, but added a term for the global parkinsonism score obtained during the same annual testing cycle as the mobility scores. In this model, both Range from TUG stand to sit (HR, 1.37, 95%CI, 1.07, 1.75) and the global parkinsonism score (HR, 2.31, 95%CI, 1.74, 3.08) were independently associated with incident parkinsonism, but Yaw from TUG turning was no longer associated (Table e1, Model 3).

To quantify the value added of sensor-derived mobility metrics, we calculated c-statistics for the previous models and compared them to a reference model with terms for demographic covariates. The model c-statistic increased as we sequentially added terms for chronic health conditions (Table e1, Model 1), sensor-derived mobility metrics, (Table e1, Model, 2) and global parkinsonism (Table e1, Model 3) suggesting that adding terms for each of these covariates improved the model prediction of incident parkinsonism.

#### **Association of wearable sensor mobility scores with incident possible parkinsonism**

Many older adults with possible parkinsonism (i.e., only 1 parkinsonian sign) progress to parkinsonism and have an increased risk of adverse health outcomes.[3] Therefore, we restricted our analyses to individuals without any signs of parkinsonism at baseline by excluding 237 of 683 (35%) subjects with 1 parkinsonian sign at baseline. We repeated the three stages of analyses described above to determine which combinations of mobility scores predict the development of possible parkinsonism.

During 2.2 years (SD=1.2, range 1 to 6 years) of follow-up, 181 out of 446 (40.6%) participants developed possible parkinsonism. In separate models, 6 out of 12 mobility scores were associated with incident possible parkinsonism (Table 4, Stage 1). Next, following backward elimination within each mobility subtask (Table 4, Stage 2), 8 mobility

We again repeated the Cox model including the four mobility scores related to incident possible parkinsonism and additionally included terms to control for chronic health conditions. Three mobility scores, including TUG sit to stand Posterior, TUG stand to sit Range, and TUG turning Yaw, remained associated with incident possible parkinsonism (Table e2, Model 2). These results were unchanged when we added terms for the severity of parkinsonism at baseline to the previous model (Table e2, Model 3).

To quantify the value added of sensor-derived mobility metrics, we calculated c-statistics for the previous models and compared them to a reference model with terms for demographic covariates. The model c-statistic increased as we sequentially added terms for chronic health conditions (Table e2, Model 1), sensor-derived mobility metrics, (Table e2, Model, 2) and global parkinsonism (Table e2, Model 3) suggesting that adding terms for each of these covariates improved the model prediction of incident possible parkinsonism.

## **DISCUSSION**

This large longitudinal study shows that sensor-derived mobility metrics recorded outside of the lab setting in the homes of older individuals predict incident parkinsonism. Further analyses of these diverse measures together in a single analytic framework identified a parsimonious combination of metrics that were independently associated with incident parkinsonism. Although gait speed, a sensitive but non-specific predictor of many adverse health outcomes [6, 26] was one of the metrics we extracted, it did not survive backward elimination and was not included in the final combination of metrics associated with incident parkinsonism. The sensor-derived mobility metrics improved the prediction of incident parkinsonism in a model which included terms for chronic health conditions and clinical severity of parkinsonism based on a modified UPDRS. These data suggest that sensor-derived mobility metrics complement conventional gait speed and clinical assessments of parkinsonism and offer the potential for identifying older adults at risk for parkinsonism to facilitate early interventions.

Parkinsonism in older adults is not synonymous with PD, but may be caused by diverse etiologies including medications, chronic medical conditions, and other neurodegenerative disorders.[2] Recent work has shown that the accumulation of diverse neurodegenerative and cerebrovascular disease pathologies are related to the severity of parkinsonism in adults without overt neurologic disease and that only a minority show evidence of PD pathology. [20, 27, 28] Regardless of its underlying causes, the societal costs and its increasing magnitude with age make the prevention of parkinsonism a public health priority. Developing clinical biomarkers which can facilitate early interventions for specific etiologies or brain pathologies to maintain ambulation in older adults is a health priority in our aging population.

In a prior cross-sectional study, we showed that the sensor-derived mobility metrics examined in this study were related to the severity of parkinsonian gait in older adults. This study extends these cross-sectional findings by showing that these metrics may identify older adults who do not currently have parkinsonism, but have an increased risk of its subsequent development. As in our prior study, some but not all of the mobility scores measured were associated with incident parkinsonism. This suggests that there may be distinct facets of mobility in older adults which are particularly salient for the development of parkinsonism. Metrics from the wearable sensor also predicted possible parkinsonism, which is an intermediate state in many adults who may transition to parkinsonism.[25] Importantly, the combinations of mobility scores at baseline which predicted possible parkinsonism and parkinsonism differed, underscoring their heterogeneity. This heterogeneity may also explain why some but not all individuals progress from possible parkinsonism to parkinsonism. Further work is needed to determine to what extent these differences in mobility score combinations might be specific to distinct underlying mechanisms of disease and how they change over time.

The results of our analyses highlight features of gait that were independently associated with incident parkinsonism. Specifically, we identified 2 mobility scores from TUG (Yaw and Range) that make significant contributions to incident parkinsonism in a joint model. These mobility scores are derived from 2 distinct motor subtasks of the TUG, highlighting these specific aspects of mobility (turning and the transition from standing to sitting) as predictors of incident parkinsonism. Interestingly, turning has long been clinically recognized as a challenging task for patients with PD and other forms parkinsonism;[29] yet, assessment of turning is not well reflected in standard clinical scales. The Yaw metric in the current study provides a quantitative measure of trunk angular velocity. The Range score of the stand to sit transition subtask was independently associated with incident parkinsonism even when controlling for the clinical severity of parkinsonism. Difficulty with initiating movements as well as smooth transitions during rapid sequential movements are both known to be particularly problematic for adults with parkinsonism due to PD or other causes.[30] Further work is needed to determine if the difficulty in transition from standing to sitting is due to difficulty in initiating movement or because of the difficulties associated with sequential movements.

This study has several limitations. Participants were selected by their willingness to participate in a clinical autopsy study. They are more highly educated and older than the general populations, making it important to replicate our findings in more diverse cohorts. It will be important to include older adults with clinical PD in further studies to determine if combinations of mobility metrics differ in parkinsonism and PD. Among the notable strengths of our study, the cohorts tested in this study provide a relatively large sample of community-dwelling older subjects with prospective data collection and uniform clinical assessments with a previously validated modified UPDRS. These encouraging results highlight the need for further work to determine whether extracting additional mobility metrics will increase the specificity of this approach, to identify older adults at risk for specific etiologies of parkinsonism and especially those who will develop PD and other synucleinopathies.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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## **Highlights**

- **•** 139 of 683 individuals (20%) developed parkinsonism during 2.5 years of follow up.
- **•** 6 of 12 sensor-based metrics at baseline are associated with incident parkinsonism.
- **•** In a combined model, 2 metrics were independently associated with parkinsonism.
- **•** Those associations were unchanged when controlling for chronic health conditions.

#### **Table 1:**

### Characteristics at Baseline, N=683



**BMI**: Body mass index; **MMSE**: Mini-Mental State Examination

### **Table 2:**

#### Baseline mobility measures derived from a wearable sensor



Mobility measures extracted from each mobility subtask, and mobility scores summarizing respective measures, as previously described.<sup>23</sup>

\* median



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Final models for each of the three stages of analyses to identify the combination of mobility scores independently related to incident parkinsonism. **HR**: hazard ratio; **CI**: confidence interval. allal 5 Final models for each of the

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**Table 3:**

Association of mobility scores with incident parkinsonism



Final models for each of the three stages of analyses to identify the combination of mobility scores independently related to incident possible parkinsonism. HR: hazard ratio; CI: confidence interval. Final models for each of the three stages of analyses to identify the combination of mobility scores independently related to incident possible parkinsonism. **HR**: hazard ratio; **CI**: confidence interval.

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**Table 4:**

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