Research Article

Different Combinations of Mobility Metrics Derived From a Wearable Sensor Are Associated With Distinct Health Outcomes in Older Adults

Aron S. Buchman, MD,^{1,2,*} Robert J. Dawe PhD,^{1,3} Sue E. Leurgans, PhD,^{1,2} Thomas A. Curran, MS,¹ Timothy Truty,¹ Lei Yu PhD,¹ Lisa L. Barnes, PhD,^{1,2,4} Jeffrey M. Hausdorff PhD,^{1,5,6,7,8} and David A. Bennett, MD^{1,2}

¹Rush Alzheimer's Disease Center, ²Department of Neurological Sciences, ³Department of Diagnostic Radiology and Nuclear Medicine, and ⁴Department of Behavioral Sciences Rush University Medical Center, Chicago, Illinois. ⁵Tel Aviv University Medical School Center for the Study of Movement, Cognition, and Mobility, Neurological Institute, Tel Aviv Medical Center, Israel. ⁶Department of Physical Therapy, Sackler Faculty of Medicine, Tel Aviv University, Israel. ⁷Sagol School of Neuroscience, Tel Aviv University, Israel. ⁸Department of Orthopedic Surgery, Rush University Medical Center, Chicago, Illinois.

*Address correspondence to: Aron S. Buchman, MD, Rush Alzheimer's Disease Center, Rush University Medical Center, 1750 West Harrison Street, Suite 1000, Chicago, IL 60612. E-mail: Aron_S_Buchman@rush.edu

Received: December 3, 2018; Editorial Decision Date: June 18, 2019

Decision Editor: Anne Newman, MD, MPH

Abstract

Background: Gait speed is a robust nonspecific predictor of health outcomes. We examined if combinations of gait speed and other mobility metrics are associated with specific health outcomes.

Methods: A sensor (triaxial accelerometer and gyroscope) placed on the lower back, measured mobility in the homes of 1,249 older adults (77% female; 80.0, *SD* = 7.72 years). Twelve gait scores were extracted from five performances, including (a) walking, (b) transition from sit to stand, (c) transition from stand to sit, (d) turning, and (e) standing posture. Using separate Cox proportional hazards models, we examined which metrics were associated with time to mortality, incident activities of daily living disability, mobility disability, mild cognitive impairment, and Alzheimer's disease dementia. We used a single integrated analytic framework to determine which gait scores survived to predict each outcome.

Results: During 3.6 years of follow-up, 10 of the 12 gait scores predicted one or more of the five health outcomes. In further analyses, different combinations of 2–3 gait scores survived backward elimination and were associated with the five outcomes. Sway was one of the three scores that predicted activities of daily living disability but was not included in the final models for other outcomes. Gait speed was included along with other metrics in the final models predicting mortality and activities of daily living disability but not for other outcomes.

Conclusions: When analyzing multiple mobility metrics together, different combinations of mobility metrics are related to specific adverse health outcomes. Digital technology enhances our understanding of impaired mobility and may provide mobility biomarkers that predict distinct health outcomes.

Keywords: Gait, Health outcomes, Wearable sensor, Aging.

Motor impairment, a common consequence of aging, may affect 50% or more of older adults by age 85 and is associated with a number of adverse health outcomes, including mortality, disabilities, mild cognitive impairment (MCI), and dementia (1). Effective prevention and interventions hinge on the early and ac-

curate identification of individuals at risk for these different adverse health outcomes.

Mobility is a complex behavior that requires coordinated rhythmic activation of diverse muscles and body segments, postural control of the moving body, and adaptation of these movements to

meet motivational and environmental demands. Gait speed describes one aspect of this complex phenotype, but does not provide specificity about which features of mobility might underlie measured slowing. This may account for the observation that gait speed is a robust, nonspecific predictor of diverse adverse health outcomes (2).

Over the past two decades, specialized gait laboratories have quantified a wide range of mobility metrics distinct from gait speed, which are necessary for successful locomotion (3–8). Measuring and summarizing these additional facets of mobility has increased our understanding of the complexity of mobility and its vital role in healthy aging (9–16). These advances in quantifying the complexity of mobility have been extended beyond specialized laboratories via instrumented testing (eg, wearable devices, gait mats, video analyses) to characterize three-dimensional gait performances more fully in other testing venues. However, despite the accumulating wealth of information about different facets of mobility, as well as the use of factor analysis to reduce the large number of measures that can be extracted (9–15), it is not known if an array of multiple metrics together can prospectively predict and discriminate between multiple adverse health outcomes. Stated differently, although it has been clearly demonstrated the gait speed predicts multiple adverse health outcomes, such as death, dementia, and disability, it is not yet known if different combinations of gait metrics that may (or may not) include gait speed predict health outcomes in distinct groups. From a biomarker and risk stratification perspective, it is important to have tools that are both sensitive (eg, gait speed) and specific (putatively the different combinations of mobility metrics).

In prior cross-sectional studies, we showed that analyzing a battery of sensor-derived mobility metrics together complement conventional gait speed and timed mobility performances to capture more diverse facets of mobility in community-based cohort studies and that different groupings of these mobility metrics were related to different clinical phenotypes (13,17–20). We have not applied our approach to longitudinal data to show if different combinations of mobility metrics are associated with specific outcomes, each with its own set of predictors. If true, this might lead to the development of distinct groupings of mobility metrics which could serve as biomarkers for distinct aging phenotypes or health outcomes.

Building on these cross-sectional findings, we used data from more than 1,200 older adults participating in two ongoing community-based cohort studies of aging (Rush Memory and Aging Project and Minority Aging Research Study) to test the hypothesis that different combinations of sensor-derived mobility metrics, including gait speed are differentially related to five specific adverse health outcomes.

Methods

Participants

Participants were drawn from two ongoing longitudinal cohort studies that use a core of common procedures for data collection by the same staff. The Rush Memory and Aging Project began in 1997 and involves annual clinical evaluations of older people in the Chicago area; participants are mostly white but approximately 6% are black (21). The Minority Aging Research Study began in 2004 and involves annual clinical evaluations of older black adults in the Chicago area recruited from the community. A body sensor worn during the annual mobility testing was added to both studies in 2012 (22). Both studies were approved by the institutional review board of Rush University Medical Center. Written informed consent was obtained from all study participants.

Eligibility for these analyses required completed mobility testing with a wearable body sensor and clinical assessment with at least one annual follow-up evaluation for these longitudinal

analyses. There were 766 (Rush Memory and Aging Project) and 483 (Minority Aging Research Study) participants included in these analyses.

Sensor-Derived Mobility Metrics

Mobility testing

Structured mobility testing was performed at each participant's residence (23,24). This testing was recorded with a wearable sensor (Dynaport MT; McRoberts B.V., the Netherlands) positioned on the lower back with a neoprene belt. 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.

Tasks tested

Three performances were evaluated. (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 (13). (b) *Timed Up and Go* (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. The TUG walking distance was limited to 8 ft (as opposed to the commonly used distance of 10 ft), in order to ensure that the task could be performed in participants' homes. In prior work, we showed that the TUG is composed of four different movements or subtasks (25,26). For this study, we focused on three TUG subtasks, including (1) *transition from sit to stand* (S1), (2) *transition from stand to sit* (S2), and (3) *turning subtasks*. The TUG walking subtask was not included so as not to duplicate the walk measures obtained from the 32-ft walk, which provided more detailed measures of gait due to the longer distance tested. (c) *Standing Posture*: Participants were asked to stand for 20 seconds in a comfortable position, with their feet about shoulder-width apart, and their eyes closed. One trial each of the 32-ft walk and the 20-second standing performances and two trials of the TUG were recorded.

Data collection and extraction of mobility measures

Collection of mobility recordings from a laptop computer is controlled by the research assistant through the use of a wireless, hand-held clicker. All three performances were recorded in a single file, with markers automatically embedded in the file to identify the beginning and the end of each performance. Mobility recordings were uploaded to a central server and analyzed at a later time.

We adapted previously validated formulas for automated analysis of large numbers of mobility recordings (25–27). These analytic tools were incorporated into a pipeline integrating data collection and the extraction of sensor-derived mobility metrics (13,17–20). Further details are summarized in the [Supplementary Methods](#).

Gait scores

As shown in [Table 1](#), we extracted 26 measures from the five mobility subtasks examined in this study. In prior work, we used available literature together with principal component analysis to summarize these measures into the 12 mobility scores, which were the primary measures used in the analyses described later.

Clinical Covariates and Adverse Health Outcomes

The annual uniform structured clinical evaluation includes a medical history and cognitive testing. Age, sex, years of education, and race were recorded at baseline interview. Body mass index was

calculated from measured weight in kilograms divided by height in meters squared. The measure is coded into four categories: underweight (<18.5), normal (18.5 to <25), overweight (25 to <30), and obese (>30). The number of three self-reported vascular risk factors (hypertension, diabetes mellitus, and smoking) and four self-reported vascular diseases (myocardial infarction, congestive heart failure, claudication, and stroke) were used in these analyses.

Mortality

When an autopsy is obtained, date of death is known promptly. When no autopsy is obtained, we obtain information on date of death from an interview with a knowledgeable informant, and very rarely with searches of public databases as a result of total loss of contact (28).

Disability

Disability was assessed annually via two self-report instruments. *Basic activities of daily living* (ADL) were assessed using six items from the Katz scale scored as 0–6 (29). *Mobility disability* was assessed using the Rosow–Breslau scale, which assesses three walking tasks, scored 0–3 (30). As in prior studies, a nonzero score was considered disabled for these analyses.

Cognitive impairment

Cognitive assessment and status was diagnosed in a three-step process. Nineteen cognitive tests were scored by a computer and summarized as a composite measure of global cognition (31). These data were reviewed by a neuropsychologist to diagnose cognitive impairment. Then participants were evaluated by a clinician who used all cognitive and clinical data to diagnose dementia status.

A clinician, experienced in the evaluation of older persons, reviewed all available data to determine a cognitive diagnosis at each visit using criteria previously described. Dementia and its causes were diagnosed using the guidelines of the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (32). Individuals with cognitive impairment who did not meet dementia criteria were diagnosed with MCI. Individuals without dementia or MCI were classified as having no cognitive impairment.

Statistical Analyses

The analytic baseline visit for this analysis is the first visit with body sensor data. We used a set of Cox proportional hazards models to examine the association of baseline sensor gait scores with continuous years to mortality, and time to the first instance of a nonzero ADL or mobility disability score and to the first instance of the diagnosis of MCI and Alzheimer's disease (AD). All models included terms for age, sex, education, and race.

The goal of our analysis was to identify which combinations of gait scores were associated with each health outcome and consisted of three stages. *Stage 1*: We examined each of the 12 gait scores individually in separate Cox proportional hazards model to determine their associations with each of the five health outcomes: mortality, ADL disability, mobility disability, MCI, and AD dementia. *Stage 2*: To determine which gait scores from each of the five mobility subtasks were associated with each health outcome, we included all gait scores of the respective subtask in one model, and used a series of Cox proportional hazards models with backward elimination. To insure that we did not exclude a potential significant association in Stage 2, gait scores were carried forward if their significance was less than .100. Stage 2 was equivalent to Stage 1 for the standing posture as this subtask was described by only one gait score, sway. *Stage 3*: To determine which

subtasks were associated with each health outcome, we included all gait scores, which survived the prior two stages, together in a series of Cox proportional hazards models with backward elimination.

In contrast to Stage 2, Stages 1 and 3 used a conventional nominal significance of $p < .05$. In order to be able to compare across outcomes, the demographic variables (age, sex, education, and race) were retained in all models and backward elimination was applied only to the gait scores. 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) and R software (33,34).

Results

A total of 1,249 participants were included in these analyses. Average age at the time of instrumented gait testing was 80.0 ($SD = 7.72$) years, with 15.1 ($SD = 3.13$) years of education and a Mini-Mental State Examination of 27.4 ($SD = 3.02$). 956 (77%) were females and 524 (42%) were black. The mobility measures extracted from each of the individual mobility subtasks that were used to construct the 12 gait scores are summarized in Table 1.

Individual Gait Scores and Incident Adverse Health Outcomes

In Stage 1 of our analysis, we examined the association of each of the 12 gait scores individually with adverse health outcomes using a series of Cox proportional hazards models that controlled for age, sex, education, and race.

Mortality

Of 1,249 participants, 222 (17.8%) died during 3.6 ($SD = 1.57$) years of follow-up. Eight of 12 gait scores including Sway, TUG Turn Yaw, TUG Stand to Sit Jerk, TUG Sit to Stand Posterior and Anterior-Posterior scores and several 32-ft walk scores (Variability, Regularity, and Speed) were associated with mortality (Table 2).

ADL disability

Of 616 participants without ADL disability at baseline, 257 (41.7%) developed incident disability more than 3.4 ($SD = 1.68$) years of follow-up. Nine gait scores including Sway, TUG Turn Yaw, TUG Stand to Sit Jerk, several TUG Sit to Stand scores (Posterior, Range, and Anterior-Posterior) and several 32-ft walk scores (Variability, Regularity, and Speed) were associated with incident ADL disability (Table 2).

Mobility disability

Of 388 without mobility disability at baseline, 217 (55.9%) developed disability more than 3.0 ($SD = 1.70$) years of follow-up. Five gait scores including TUG Turn Yaw, TUG Stand to Sit Jerk, TUG Sit to Stand Posterior and Anterior-Posterior scores and 32-ft walk Speed score were associated with incident mobility disability (Table 2).

Mild cognitive impairment

Of 900 with no cognitive impairment at baseline, 226 (25.1%) developed MCI during 3.2 ($SD = 1.44$) years of follow-up. Two gait scores from the 32-ft walk including Regularity and Cadence scores were associated with incident MCI (Table 2).

Alzheimer's dementia

Of 1,019 individuals without dementia at baseline (900 no cognitive impairment and 119 MCI), 96 (9.4%) developed dementia during

Table 1. Wearable Mobility Metrics at Study Baseline

Tasks	Mobility Subtasks	Individual Gait Measures Extracted			Gait Scores
		Measure (units)	Mean (SD)	Q1, Q3	
Standing Eyes Closed	Standing Posture	Total power (PSD)	0.56 (0.913)	0.16, 0.59	Sway
		RMS distance (g)	0.15 (0.112)	0.10, 0.17	
TUG	TUG Turn	Jerk (g/s)	0.05 (0.185)	0.01, 0.03	Turn Frequency
		Frequency, turn (Hz)	1.65 (0.691)	0.98, 2.34	
		Yaw duration, turn 2 (s)	2.09 (0.707)	1.63, 2.40	
	TUG Transition Stand to Sit	Yaw amplitude, turn (deg/s)	143.76 (42.552)	111.72, 173.29	Range
		AP Acceleration SD (g)	0.30 (0.079)	0.24, 0.35	
		Pitch range (deg/s)	160.90 (51.035)	126.04, 186.45	
		AP range (g)	1.08 (0.370)	0.85, 1.22	
		AP jerk (g/s)	1.34 (3.071)	0.70, 1.42	
		Pitch duration (s)	1.11 (0.478)	0.77, 1.33	
	TUG Transition Sit to Stand	AP duration (s)	1.00 (0.544)	0.65, 1.21	Jerk
		Pitch jerk (deg/s ²)	149.76 (90.384)	89.19, 189.64	
		Pitch duration (s)	0.90 (0.370)	0.65, 1.05	
		Pitch jerk (deg/s ²)	199.85 (102.725)	123.50, 260.26	
		Pitch range (deg/s)	168.70 (53.143)	133.56, 197.37	
		AP Acceleration SD (g)	0.30 (0.086)	0.24, 0.35	
32-ft Walk	32-ft Walk	AP range (g)	1.07 (0.393)	0.82, 1.24	Anterior-Posterior
		AP jerk (g/s)	-1.45 (2.525)	-1.80, -0.67	
		AP duration (s)	0.95 (0.688)	0.54, 1.13	
		Step symmetry	1.39 (0.433)	1.15, 1.59	
		Stride regularity (g ²)	0.28 (0.108)	0.21, 0.35	
		Stride time CV (%)	3.99 (1.856)	2.75, 4.77	
		Cadence (steps/min)	56.09 (10.802)	49.41, 62.46	
		Stride length (m)	0.88 (0.291)	0.70, 0.98	
		Speed (m/s)	0.75 (0.102)	0.70, 0.82	

Notes: The individual measures extracted using custom-designed software from each of the five mobility subtasks and how those measures were combined to form composite gait scores. The axes for the acceleration measurements were vertical (V), mediolateral (ML), and anterior-posterior (AP); and the axes for the rotational velocities were yaw (rotation about vertical axis), pitch (rotation about ML axis), and roll (rotation about AP axis). For the standing posture subtasks, total power is the integrated power spectrum, root mean square (RMS) quantifies the magnitude of the acceleration, and jerk is the time derivative of the acceleration or rotational velocity in the specified axis, between the maximum and minimum points. For the turn subtasks, frequency represents the dominant frequency in the AP acceleration during the turn. For the transition subtasks, time duration, range, and pitch are independently calculated from both the Pitch and AP signals. Step and stride symmetry are calculated from the autocorrelation of the vertical acceleration. Step symmetry reflects left-right stepping differences and is defined as the step regularity divided by stride regularity (see [Supplementary Methods](#) for additional details). CV = coefficient of variation; TUG = Timed Up and Go.

3.4 ($SD = 1.38$) years of follow-up. Four gait scores including TUG Turn Yaw score and several scores from the 32-ft walk Regularity and Speed were associated with incident AD ([Table 2](#)).

Combinations of Gait Scores and Incident Adverse Health Outcomes

The results of the backward elimination process that was applied in Stage 2 to determine which gait scores within each of the subtasks were associated with each of the adverse health outcomes are summarized in [Table 3](#).

In Stage 3 of our analysis, the gait scores from the five mobility subtasks that survived the first two stages were all included in a single model to determine which gait scores remained associated with each of the five health outcomes. [Table 4](#) shows the results for the third stage of the analysis in which different combinations of two or three gait scores were associated with each of the specific, individual health outcomes. These combinations were unchanged when we added terms for body mass index, self-reported chronic vascular risk factors and diseases to each of the five models in [Table 4](#) (results not shown).

Given the large number of comparisons, we examined if the previous results ([Table 4](#)) were changed if we applied a stricter threshold and used less than 0.01 as the level of significance. The combinations

predicting mortality, ADL disability, and AD dementia were unchanged ([Table 4](#)). However, several TUG gait scores predicting mobility disability and walk regularity predicting incident MCI were no longer significant ([Table 4](#)). Nonetheless, gait scores remained differentially associated with adverse health outcomes. These results were unchanged when we excluded individuals ($N = 7$) with a history of clinical Parkinson's disease (results not shown).

Discussion

New technologies yield large quantities of data describing different facets of human biology, that is, genomics and wearable devices for clinical phenotypes, such as mobility. Integrative methods are critical for showing the added value of these data ([35](#)). As we and others have done in prior work, we derived multiple mobility measures including gait speed from wearable sensor recordings obtained from short, structured mobility testing in the residences of more than 1,200 ambulatory older adults and used factor analysis to reduce the multiple measures extracted. In contrast, to prior studies, we modeled this battery of multiple mobility metrics together in a single analytic framework to examine the prospective association of these diverse metrics with different adverse health outcomes. Interestingly,

Table 2. Individual Gait Scores Associated With Incident Adverse Health Outcomes

Subtask	Gait Scores	Mortality		ADL Disability		Mobility Disability		MCI		AD Dementia	
		HR (CI)	p Value	HR (CI)	p Value	HR (CI)	p Value	HR (CI)	p Value	HR (CI)	p Value
Standing Posture TUG Turn	Sway	1.21 (1.06, 1.37)	.005	1.21 (1.06, 1.38)	.004	1.10 (0.95, 1.28)	.204	1.13 (0.98, 1.32)	.102	0.97 (0.78, 1.19)	.744
	Frequency	1.01 (0.86, 1.17)	.962	0.98 (0.83, 1.15)	.773	1.05 (0.88, 1.26)	.578	1.06 (0.90, 1.25)	.488	0.90 (0.72, 1.12)	.346
	Yaw	0.58 (0.48, 0.71)	<.001	0.39 (0.31, 0.48)	<.001	0.52 (0.41, 0.67)	<.001	0.89 (0.73, 1.07)	.222	0.68 (0.52, 0.90)	0.006
TUG Stand to Sit	Range	1.08 (0.91, 1.28)	.402	0.90 (0.75, 1.07)	.240	1.06 (0.87, 1.29)	.588	0.97 (0.81, 1.16)	.722	1.03 (0.80, 1.32)	.824
	Jerk	0.83 (0.70, 0.99)	.042	0.63 (0.52, 0.76)	<.001	0.73 (0.59, 0.90)	.004	0.99 (0.82, 1.19)	.917	0.96 (0.75, 1.24)	.759
	Posterior	0.65 (0.56, 0.76)	<.001	0.68 (0.57, 0.79)	<.001	0.80 (0.67, 0.97)	.020	0.95 (0.82, 1.11)	.526	1.08 (0.87, 1.33)	.489
TUG Sit to Stand	Range	0.87 (0.73, 1.05)	0.145	0.82 (0.68, 0.996)	.046	1.07 (0.88, 1.31)	.503	0.96 (0.82, 1.15)	.661	0.80 (0.61, 1.04)	.094
	Ant-Post	0.73 (0.64, 0.85)	<.001	0.75 (0.64, 0.88)	<.001	0.80 (0.67, 0.95)	.012	1.10 (0.95, 1.27)	.205	1.03 (0.38, 1.27)	0.779
	Variability	0.78 (0.69, 0.89)	<.001	0.81 (0.70, 0.93)	.004	0.97 (0.84, 1.12)	.709	0.92 (0.80, 1.06)	0.251	0.73 (0.60, 0.90)	.002
32-ft Walk	Regularity	0.74 (0.64, 0.87)	<.001	0.76 (0.63, 0.88)	<.001	0.95 (0.78, 1.16)	.626	0.82 (0.70, 0.98)	.027	0.68 (0.54, 0.86)	.001
	Cadence	0.90 (0.79, 1.02)	.104	1.06 (0.93, 1.20)	.421	1.00 (0.86, 1.16)	.996	1.17 (1.02, 1.33)	.025	1.08 (0.89, 1.30)	.425
	Speed	0.54 (0.45, 0.64)	<.001	0.38 (0.30, 0.48)	<.001	0.62 (0.48, 0.81)	<.001	0.87 (0.71, 1.06)	.170	0.62 (0.47, 0.81)	<.001

Notes: Each cell shows a hazard ratio (HR), 95% confidence interval (CI), p value for a single Cox model examining the association of each of the 12 gait scores with each of the adverse health outcome shown. All models also included terms for demographics variables, which are not shown. AD = Alzheimer's disease; ADL = Activities of daily living; MCI = Mild cognitive impairment; TUG = Timed Up and Go.

Table 3. Gait Scores Within Subtasks Associated With Incident Adverse Health Outcomes

Subtask	Gait Scores	Mortality		ADL Disability		Mobility Disability		MCI		AD Dementia	
		HR (CI)	p Value	HR (CI)	p Value	HR (CI)	p Value	HR (CI)	p Value	HR (CI)	p Value
Standing Posture TUG Turn	Sway	1.21 (1.06, 1.37)	.005	1.21 (1.06, 1.38)	.004	—	—	—	—	—	—
	Frequency	—	—	—	—	—	—	—	—	—	—
	Yaw	0.57 (0.46, 0.69)	<.001	0.39 (0.32, 0.50)	<.001	0.52 (0.40, 0.67)	<.001	—	—	0.66 (0.50, 0.89)	.006
TUG Stand to Sit	Range	1.17 (0.98, 1.41)	.089	—	—	1.28 (1.02, 1.60)	.035	—	—	—	—
	Jerk	0.79 (0.65, 0.95)	.012	0.63 (0.52, 0.76)	<.001	0.65 (0.51, 0.83)	<.001	—	—	—	—
	Posterior	0.71 (0.61, 0.84)	<.001	0.71 (0.60, 0.84)	<.001	0.80 (0.67, 0.97)	.064	—	—	—	—
TUG Sit to Stand	Range	—	—	—	—	1.21 (0.978, 1.51)	.085	—	—	—	—
	Ant-Post	0.83 (0.70, 0.98)	.024	0.82 (0.70, 0.97)	.023	0.77 (0.63, 0.94)	.009	—	—	—	—
	Variability	—	—	—	—	—	—	—	—	—	—
32-ft Walk	Regularity	0.83 (0.71, 0.97)	.021	—	—	—	—	0.80 (0.67, 0.96)	.013	0.72 (0.57, 0.91)	.006
	Cadence	—	—	—	—	—	—	1.20 (1.05, 1.37)	.009	—	—
	Speed	0.56 (0.47, 0.66)	<.001	0.38 (0.30, 0.48)	<.001	0.62 (0.48, 0.81)	<.001	—	—	0.68 (0.51, 0.81)	.008

Notes: All 12 gait scores were included in the initial model which examined which of the gait scores for each of the subtasks shown in the left hand column were associated with the adverse health outcome at the top of each column. Each cell shows a hazard ratio (HR), 95% confidence interval (CI), p value for gait scores associated with the adverse health outcomes listed at the top of each of the column. Cells with a dash (—) show gait scores that were unrelated to an adverse health outcome and did not survive backward elimination. All models also included terms for demographics variables, which are not shown. AD = Alzheimer's disease; ADL = Activities of daily living; MCI = Mild cognitive impairment; TUG = Timed Up and Go.

Table 4. Combinations of Gait Scores Associated With Incident/Adverse Health Outcomes

Subtask	Gait Scores	Mortality			ADL Disability			Mobility Disability			MCI			AD Dementia		
		HR (CI)	p Value		HR (CI)	p Value		HR (CI)	p Value		HR (CI)	p Value		HR (CI)	p Value	
Standing Posture TUG Turn	Sway	—	—		1.22 (1.05, 1.41)	.008		—	—		—	—		—	—	
	Frequency	—	—		—	—		—	—		—	—		—	—	
	Yaw	—	—		0.52 (0.40, 0.68)	<.001		0.47 (0.36, 0.63)	<.001		—	—		0.67 (0.50, 0.89)	.006	
TUG Stand to Sit	Range	—	—		—	—		—	—		—	—		—	—	
	Jerk	—	—		—	—		—	—		—	—		—	—	
	Posterior	—	—		—	—		—	—		—	—		—	—	
TUG Sit to Stand	Range	0.77 (0.65, 0.92)	.003		—	—		1.33 (1.06, 1.67)	0.015		—	—		—	—	
	Ante-Post	—	—		—	—		0.80 (0.64, 0.99)	0.037		—	—		—	—	
	Variability	—	—		—	—		—	—		—	—		—	—	
32-ft Walk	Regularity	—	—		—	—		—	—		—	—		—	—	
	Cadence	—	—		—	—		—	—		—	—		—	—	
	Speed	—	—		—	—		—	—		—	—		—	—	
Final Gait Score Combinations	Speed	0.50 (0.40, 0.64)	<.001		0.59 (0.43, 0.82)	.002		—	—		0.80 (0.67, 0.96)	.013		0.71 (0.56, 0.91)	.008	
	TUG Sit to Stand-Post	—	—		Posture-Sway	—		TUG Turn-Yaw	—		Walk-Regularity	—		TUG Turn-Yaw	—	
	Walk-Speed	—	—		TUG Turn-Yaw	—		TUG Sit to Stand-Range	—		Walk-Cadence	—		Walk-Regularity	—	
					Walk-Speed	—		TUG Sit to Stand-Ant-Post	—			—			—	

Notes: Each column in this table shows the results for a single Cox model for each of the five outcomes examined in Stage 3. Gait scores included in each model were based on gait scores for each subtask, which remained significant following Stage 1 and 2. The gait scores included the initial model for each column shows a hazard ratio (HR), 95% confidence interval (CI), and p value for those scores survived backward elimination and remained associated with the adverse health outcomes listed at the top of the columns. Cells with a dash (—) show gait scores that were included in the initial model for Stage 3, but did not survive backward elimination. Completely blank cells with no HR or dash (—) did not survive Stage 1 or 2 and were not associated with the outcome at the top of the column. All five models also included terms for demographics variables (eg, age, sex), which are not shown (see the Methods section for further details). AD = Alzheimer's disease; ADL = Activities of daily living; MCI = Mild cognitive impairment; TUG = Timed Up and Go.

we found that these metrics predict adverse health outcomes and that different groupings of these metrics were related to five specific health outcomes (mortality, disability in ADL, mobility disability, MCI, and Alzheimer's dementia). These results are an important step toward an approach that leverages the large quantities of mobility data derived from digital technologies to enhance prognosis, quantify risk, and investigate mechanisms underlying impaired mobility in older adults. These findings also illustrate the potential not only to enhance our understanding of common aging phenotypes like impaired mobility but for developing clinical mobility signatures or biomarkers which may improve risk stratification for specific adverse health outcomes.

For each performance assessed, the body-fixed sensor provides a speed or duration metric that is analogous to a conventional measure obtained via a stopwatch. In addition, sensor-derived mobility metrics also quantify other facets of these same performances. Prior cross-sectional studies suggest that these additional metrics may also inform on which aspect of mobility may contribute to performance slowing or other features of impaired mobility (13,17–20). Such information is crucial for untangling the varied mechanisms, etiologies, and pathways that can lead to impaired mobility and offer the potential for targeted interventions.

The results of the analyses from the first stage of this study extend our previous cross-sectional studies by showing that nearly all of the mobility metrics derived from a wearable body sensor in the community setting are also associated with the subsequent development of one or more adverse health outcomes in older adults (Table 2) (6,13,17–19,36). These results complement prior studies that have shown that timed tasks such as gait speed are sensitive, but nonspecific predictors of diverse adverse health outcomes (2).

To take full advantage of the multiple mobility metrics obtained from wearable technologies, we used a single integrated analytic framework. On the basis of our prior cross-sectional work, we reasoned that using a larger battery of mobility metrics and analyzing them together might discriminate or reflect different health outcomes. In our analyses that included gait speed and other gait scores together, stepwise Cox models with backward elimination were used to exclude gait scores that might not be related to a health outcome when considered together with other mobility metrics. We found that different combinations or groupings of gait scores were associated with specific health outcomes (Table 4). For example, sway was an independent predictor of ADL disability but was not included in the final models of other health outcomes. Stride regularity, a measure of stride-to-stride consistency, was an independent predictor of mortality, MCI, and AD, but not mobility disability. Aspects of mobility not routinely assessed including angular velocity of the trunk, a measure that reflects trunk rotation, during turn, and transition from sit to stand were independent predictors of disability and mortality. Initial models for all the health outcomes included gait speed. However, gait speed did not always survive backward elimination to be included in the final models (eg, mobility disability, MCI, and AD). Even when gait speed survived backward elimination, other measures would only be included if they provided additional predictive value. These findings have important implications for using mobility as a “bio-marker” as these data suggest that measuring a battery of metrics together may provide a more comprehensive characterization of mobility and account for the differential associations of mobility metrics with the specific health outcomes examined (eg, dementia vs death). Further work with alternative variable selection approaches may provide the means to compare and cross-validate results from the approach used in this study. Developing several complementary variable selection approaches and correcting for

multiple comparisons may prove especially useful for the increasingly complex analyses of the large numbers of measures that can be obtained from simultaneous recordings of multiple wearable devices.

The biology underlying the associations of different combinations of mobility metrics with distinct adverse health outcomes is unclear. Combinations of mobility metrics may represent biomarkers for different health outcomes. Thus, if these combinations of mobility metrics are replicated in other cohorts, these metrics can potentially be combined with other clinical, laboratory, and imaging covariates for the development of clinical profiles that provide more accurate risk stratification of older adults for specific health outcomes. Although further work is needed, the present results also provide important clues about the underlying facets of mobility preferentially associated with specific adverse health outcomes. For example, sway was only associated with disability. Although turn was a sensitive indicator for MCI in a cross-sectional study, walk measures were associated with incident MCI but not the turn score (18). Moreover, gait scores predicting MCI and AD were different. Finally, gait speed metrics as well as transition from sit to stand predicted mortality, which might underscore the importance of ongoing walking as a predictor of survival in older adults. Mobility is a complex behavior that is derived from dissociable neural systems with spatially distinct networks, which regulate different facets of mobility. Just as the biology leading to different adverse health outcomes varies, the different combinations of gait scores may capture salient deficits within neural and nonneural systems underlying different aspects of mobility. Thus, these combinations may not only improve risk stratification among older adults, but further work has the potential to identify candidates for targeted interventions for different adverse health outcomes.

The results of this study are promising, but several of its limitations highlight that further work is necessary to develop mobility signatures or biomarkers for clinical use. The mobility metrics obtained in this study were derived from three tasks, so extracting more diverse metrics from additional performances could further improve the specificity of predictions for distinct adverse health outcomes. Recent work has highlighted the importance of developing consensus on the type, scope of measures, and optimal venue for collecting digital health measures (23,24). This study used short, structured supervised testing sessions that assessed only a limited number of mobility performances and was constrained by the instructions of the tester. In contrast, everyday mobility is typically “unsupervised” and movement is adapted to meet the diverse motivational and environmental demands during the course of daily living. Structured supervised testing may not reflect how older adults move in everyday living (23,24,37). Multiday mobility recordings of everyday living may provide important data about movement planning and control strategies employed by older adults as they adapt to environmental and contextual cues when moving during daily living. Using metrics obtained from both structured testing with metrics and everyday mobility might improve the predictions of mobility signatures for risk stratification of older adults (38–40). Further, mobility is a complex construct and measurement of other salient physiologic systems that underlie gait and balance recordings such as musculoskeletal, peripheral nerve, and joint dynamics during ambulation and chronic health conditions is likely to further improve risk stratification of adverse health outcomes. Finally, we used two volunteer cohorts of community-dwelling adults who may not be representative of the general population, so the results need to be confirmed in other cohorts.

The strengths of this study include the use of a wearable device that measured both acceleration and angular velocity in three

planes to quantify several commonly assessed mobility performances including gait speed metrics in a relatively large number of men and women tested in their homes. Our approach is well anchored in the prior literature. Testing was done in the community setting that facilitates the assessment of a wider range of clinical aging phenotypes as frail older adults unable to travel outside their homes were included. Five important adverse health outcomes were examined in a single analytic cohort and prospectively.

Conclusion

Analogous to genomics and other omics, advances in wearable technologies provide the opportunity for both clinicians and researchers to leverage large novel data to increase our understanding of mobility and obtain a more comprehensive assessment of mobility outside the confines of specialized laboratories. More routine use of digital technology to record a wider range of mobility metrics in the outpatient and community setting may transform the clinical categorization of impaired mobility and understanding its varied causes in older adults. Moreover, the current results suggest that modeling combinations of diverse mobility metrics together may yield mobility “signatures” that are differentially associated with specific health outcomes. Further work to optimize the characterization of mobility and integrating these novel metrics with imaging, genomic data, and serum or laboratory biomarkers could lead to mobility signatures that improve risk stratification and allow early interventions to forestall mobility impairments and maintain ambulation in our aging population.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

Funding

This work was supported by National Institute of Health (R01AG17917 to D.A.B., RF1AG22018 to L.L.B., R01NS78009 to A.S.B., R01AG56352 to A.S.B.); the Illinois Department of Public Health (D.A.B.); and the Robert C. Borwell Endowment Fund (D.A.B.).

Acknowledgments

We thank all the participants in the Rush Memory and Aging Project and Minority Aging Research Study. We also thank the staff of the Rush Alzheimer's Disease Center. All data included in these analyses are available via the Rush Alzheimer's Disease Center Research Resource Sharing Hub, which can be found at www.radc.rush.edu. It has descriptions of the studies and available data. Any qualified investigator can create an account and submit requests for deidentified data.

Conflict of Interest Statement

None reported.

References

1. Rosso AL, Studenski SA, Chen WG, et al. Aging, the central nervous system, and mobility. *J Gerontol A Biol Sci Med Sci*. 2013;68:1379–1386. doi:10.1093/gerona/glt089
2. Abellan van Kan G, Rolland Y, Andrieu S, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people: an International Academy on Nutrition and Aging (IANA) Task Force. *J Nutr Health Aging*. 2009;13:881–889. doi:10.1007/s12603-009-0246-z

3. Doheny EP, Fan CW, Foran T, Greene BR, Cunningham C, Kenny RA. An instrumented sit-to-stand test used to examine differences between older fallers and non-fallers. *Conf Proc IEEE Eng Med Biol Soc.* 2011;2011:3063–3066. doi:10.1109/IEMBS.2011.6090837
4. Najafi B, Aminian K, Loew F, Blanc Y, Robert PA. Measurement of stand-sit and sit-stand transitions using a miniature gyroscope and its application in fall risk evaluation in the elderly. *IEEE Trans Biomed Eng.* 2002;49:843–851. doi:10.1109/TBME.2002.800763
5. Salarian A, Zampieri C, Horak FB, Carlson-Kuhta P, Nutt JG, Aminian K. Analyzing 180 degrees turns using an inertial system reveals early signs of progression of Parkinson's disease. *Conf Proc IEEE Eng Med Biol Soc.* 2009;2009:224–227. doi:10.1109/IEMBS.2009.5333970
6. Weiss A, Brozgol M, Dorfman M, et al. Does the evaluation of gait quality during daily life provide insight into fall risk? A novel approach using 3-day accelerometer recordings. *Neurorehabil Neural Repair.* 2013;27:742–752. doi:10.1177/1545968313491004
7. Montero-Odasso M, Speechley M, Muir-Hunter SW, et al.; Canadian Gait and Cognition Network. Motor and cognitive trajectories before dementia: results from gait and brain study. *J Am Geriatr Soc.* 2018;66:1676–1683. doi:10.1111/jgs.15341
8. Hubble RP, Naughton GA, Silburn PA, Cole MH. Wearable sensor use for assessing standing balance and walking stability in people with Parkinson's disease: a systematic review. *PLoS One.* 2015;10:e0123705. doi:10.1371/journal.pone.0123705
9. Verghese J, Wang C, Lipton RB, Holtzer R, Xue X. Quantitative gait dysfunction and risk of cognitive decline and dementia. *J Neurol Neurosurg Psychiatry.* 2007;78:929–935. doi:10.1136/jnnp.2006.106914
10. Hollman JH, McDade EM, Petersen RC. Normative spatiotemporal gait parameters in older adults. *Gait Posture.* 2011;34:111–118. doi:10.1016/j.gaitpost.2011.03.024
11. Lord S, Galna B, Verghese J, Coleman S, Burn D, Rochester L. Independent domains of gait in older adults and associated motor and nonmotor attributes: validation of a factor analysis approach. *J Gerontol A Biol Sci Med Sci.* 2013;68:820–827. doi:10.1093/gerona/gls255
12. Verlinden VJ, van der Geest JN, Hofman A, Ikram MA. Cognition and gait show a distinct pattern of association in the general population. *Alzheimers Dement.* 2014;10:328–335. doi:10.1016/j.jalz.2013.03.009
13. Buchman AS, Leurgans SE, Weiss A, et al. Associations between quantitative mobility measures derived from components of conventional mobility testing and Parkinsonian gait in older adults. *PLoS One.* 2014;9:e86262. doi:10.1371/journal.pone.0086262
14. Arcolin I, Corna S, Giardini M, Giordano A, Nardone A, Godi M. Proposal of a new conceptual gait model for patients with Parkinson's disease based on factor analysis. *Biomed Eng Online.* 2019;18:70. doi:10.1186/s12938-019-0689-3
15. De Cock AM, Fransen E, Perkisas S, et al. Comprehensive quantitative spatiotemporal gait analysis identifies gait characteristics for early dementia subtyping in community dwelling older adults. *Front Neurol.* 2019;10:313. doi:10.3389/fneur.2019.00313
16. Del Din S, Godfrey A, Rochester L. Validation of an accelerometer to quantify a comprehensive battery of gait characteristics in healthy older adults and Parkinson's disease: toward clinical and at home use. *IEEE J Biomed Health Inform.* 2016;20:838–847. doi:10.1109/JBHI.2015.2419317
17. Weiss A, Mirelman A, Giladi N, et al. Transition between the Timed Up and Go turn to sit subtasks: is timing everything? *J Am Med Dir Assoc.* 2016;17:864.e9–864.e15. doi:10.1016/j.jamda.2016.06.025
18. Mirelman A, Weiss A, Buchman AS, Bennett DA, Giladi N, Hausdorff JM. Association between performance on Timed Up and Go subtasks and mild cognitive impairment: further insights into the links between cognitive and motor function. *J Am Geriatr Soc.* 2014;62:673–678. doi:10.1111/jgs.12734
19. Weiss A, Mirelman A, Buchman AS, Bennett DA, Hausdorff JM. Using a body-fixed sensor to identify subclinical gait difficulties in older adults with IADL disability: maximizing the output of the Timed Up and Go. *PLoS One.* 2013;8:e68885. doi:10.1371/journal.pone.0068885
20. Dawe RJ, Leurgans SE, Yang J, et al. Association between quantitative gait and balance measures and total daily physical activity in community-dwelling older adults. *J Gerontol A Biol Sci Med Sci.* 2018;73:636–642. doi:10.1093/gerona/glx167
21. Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA. Religious Orders Study and Rush Memory and Aging Project. *J Alzheimers Dis.* 2018;64(suppl 1):S161–S189. doi:10.3233/JAD-179939
22. Barnes LL, Shah RC, Aggarwal NT, Bennett DA, Schneider JA. The Minority Aging Research Study: ongoing efforts to obtain brain donation in African Americans without dementia. *Curr Alzheimer Res.* 2012;9:734–745. doi:10.2174/156720512801322627
23. Espay AJ, Hausdorff JM, Sánchez-Ferro Á, et al.; Movement Disorder Society Task Force on Technology. A roadmap for implementation of patient-centered digital outcome measures in Parkinson's disease obtained using mobile health technologies. *Mov Disord.* 2019;34:657–663. doi:10.1002/mds.27671
24. Hillel I, Gazit E, Nieuwboer A, et al. Is every-day walking in older adults more analogous to dual-task walking or to usual walking? Elucidating the gaps between gait performance in the lab and during 24/7 monitoring. *Eur Rev Aging Phys Act.* 2019;16:6. doi:10.1186/s11556-019-0214-5
25. Weiss A, Herman T, Plotnik M, Brozgol M, Maidan I, Giladi N, et al. Can an accelerometer enhance the utility of the Timed Up & Go Test when evaluating patients with Parkinson's disease? *Med Eng Phys.* 2010;32:119–125. doi:10.1016/j.medengphy.2009.10.015
26. Weiss A, Herman T, Plotnik M, Brozgol M, Giladi N, Hausdorff JM. An instrumented Timed Up and Go: the added value of an accelerometer for identifying fall risk in idiopathic fallers. *Physiol Meas.* 2011;32:2003–2018. doi:10.1088/0967-3334/32/12/009
27. Matinoli M, Korpelainen JT, Korpelainen R, Sotaniemi KA, Virranenmi M, Myllylä VV. Postural sway and falls in Parkinson's disease: a regression approach. *Mov Disord.* 2007;22:1927–1935. doi:10.1002/mds.21633
28. Buchman AS, Yu L, Boyle PA, Shah RC, Bennett DA. Total daily physical activity and longevity in old age. *Arch Intern Med.* 2012;172:444–446. doi:10.1001/archinternmed.2011.1477
29. Katz S, Akpom CA. A measure of primary sociobiological functions. *Int J Health Serv.* 1976;6:493–508. doi:10.2190/UURL-2RYU-WRYD-EY3K
30. Rosow I, Breslau N. A Guttman health scale for the aged. *J Gerontol.* 1966;21:556–559.
31. Bennett DA, Schneider JA, Buchman AS, Barnes LL, Boyle PA, Wilson RS. Overview and findings from the Rush Memory and Aging Project. *Curr Alzheimer Res.* 2012;9:646–663. doi:10.2174/156720512801322663
32. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology.* 1984;34:939–944. doi:10.1212/wnl.34.7.939
33. SAS Institute Inc. *SAS/STAT® User's Guide, Version 9.3.* Cary, NC: SAS Institute Inc; 2012.
34. R Core Team. *R: A Language and Environment for Statistical Computing.* Vienna, Austria: R Foundation for Statistical Computing; 2017.
35. Zitnik M, Nguyen F, Wang B, Leskovec J, Goldenberg A, Hoffman MM. Machine learning for integrating data in biology and medicine: principles, practice, and opportunities. *Inf Fusion.* 2019;50:71–91. doi:10.1016/j.inffus.2018.09.012
36. Mirelman A, Gurevich T, Giladi N, Bar-Shira A, Orr-Urtreger A, Hausdorff JM. Gait alterations in healthy carriers of the LRRK2 G2019S mutation. *Ann Neurol.* 2011;69:193–197. doi:10.1002/ana.22165
37. Kaye JA, Maxwell SA, Mattek N, et al. Intelligent Systems For Assessing Aging Changes: home-based, unobtrusive, and continuous assessment of aging. *J Gerontol B Psychol Sci Soc Sci.* 2011;66(suppl 1):i180–i190. doi:10.1093/geronb/gbq095
38. Weiss A, Sharifi S, Plotnik M, van Vugt JP, Giladi N, Hausdorff JM. Toward automated, at-home assessment of mobility among patients with Parkinson disease, using a body-worn accelerometer. *Neurorehabil Neural Repair.* 2011;25:810–818. doi:10.1177/1545968311424869
39. Lowe SA, Ólaighin G. Monitoring human health behaviour in one's living environment: a technological review. *Med Eng Phys.* 2014;36:147–168. doi:10.1016/j.medengphy.2013.11.010
40. Del Din S, Godfrey A, Mazzà C, Lord S, Rochester L. Free-living monitoring of Parkinson's disease: lessons from the field. *Mov Disord.* 2016;31:1293–1313. doi:10.1002/mds.26718