

# Mobility Deviations in Adults With Human Immunodeficiency Virus: A Cross-Sectional Assessment Using Gait Analysis, Functional Performance, and Self-Report

Karina Berner,<sup>1,✉</sup> Arnaud Gouelle,<sup>2,3,✉</sup> Hans Strijdom,<sup>4,✉</sup> M. Faadiel Essop,<sup>5,✉</sup> Ingrid Webster,<sup>4,✉</sup> and Quinette Louw<sup>1,✉</sup>

<sup>1</sup>Division of Physiotherapy, Department of Health and Rehabilitation Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, <sup>2</sup>Gait and Balance Academy, ProtoKinetics, Havertown, Pennsylvania, USA, <sup>3</sup>Laboratory Performance, Santé, Métrologie, Société, UFR STAPS, (Unit for Teaching and Research - Sciences and Techniques for Physical Activities and Sports), Reims, France, <sup>4</sup>Centre for Cardio-metabolic Research in Africa, Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa, <sup>5</sup>Centre for Cardio-metabolic Research in Africa, Department of Physiological Sciences, Faculty of Science, Stellenbosch University, Cape Town, South Africa

**Background.** Little is known about how human immunodeficiency virus (HIV) affects walking biomechanics, or about associations between HIV-related gait deviations, functional performance, and self-reported outcomes. This paper reports on (1) gait biomechanics and variability in people with HIV (PWH) and (2) associations with clinical tests, self-reported function, and falls.

**Methods.** A cross-sectional study tested consecutively sampled PWH (n = 50) and HIV-seronegative participants ([SNP] n = 50). Participants underwent 3-dimensional gait analysis, performed clinical tests (short walk and single leg stance tests with and without dual tasking, chair-rise tests, and a physical performance battery), and completed questionnaires about function and falls. Between-group comparisons were done using analysis of covariance. Linear correlations between gait variability, clinical tests, and patient-reported outcomes were established.

**Results.** People with HIV and SNP had comparable median ages (PWH = 36.6, interquartile range [IQR] = 32.0–45.6]; SNP = 31.1, IQR = 23.2–45.1). Compared with SNP, PWH walked slower (adjusted mean difference [MD] = –0.2 meters per second [m/s], 95% confidence interval [CI] = –0.3 to –0.1) with greater variability (adjusted MD = 14.7 variability score points, 95% CI = 9.9–19.5). Moreover, PWH were slower in five-times sit-to-stand (5STS) performance (adjusted MD = 1.9 seconds, 95% CI = 1.00–2.9). Significant deviations in hip kinematics (increased flexion; adjusted MDs = 2.4°–2.8°, *P* = .012–.016) and knee kinematics (reduced flexion; adjusted MDs = 2.3°–3.7°, *P* = .007–.027) were found in PWH during dual-task (DT) walking. The PWH's 5STS moderately correlated with larger gait variability (usual pace *r* = –0.5; dual task *r* = –0.6), poorer self-reported mobility (*r* = 0.4) and self-care function (*r* = 0.5), and fear of falling (*P* = .003).

**Conclusions.** People with HIV presented with biomechanical deviations suggestive of a slowed and variable gait, especially under cognitive challenges. Five-times STS may be useful to screen for gait deviations in PWH.

**Keywords.** chair rise time; gait variability; HIV infection; kinematics; physical function.

There has been growing recognition of human immunodeficiency virus (HIV)-associated morbidity, including declining function, impaired lower limb performance, and gait deviations [1]. A recent systematic review concluded that middle-aged PWH can present with gait impairments resembling those of much older people with previous falls [2]. Neuromotor

impairments in PWH can result from many factors, including persistent low-grade inflammation, cellular senescence, and physiologic decline, which can accelerate aging and hasten geriatric syndromes such as falls by 10–15 years [3]. Lower limb impairment in PWH have been associated with poorer quality of life (QOL), reduced independence [3], future disability, and earlier mortality [4]. This can negatively affect health, work productivity, and healthcare utilization across the lifespan and will require long-term, potentially costly care unless early risk detection strategies can be developed.

Three-dimensional gait analysis (3DGA) sensitively detects changes in movement quality that may be subtle [5, 6]. There has been no research into how HIV affects gait biomechanics [2], or whether biomechanical deviations in PWH relate to declining function [7]. Because 3DGA can sensitively quantify the dynamic implications of impairments during a functional activity such as gait, it may be appropriate to detect early subtle

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Correspondence: Karina Berner, PhD, MSc, BSc, Division of Physiotherapy, Department of Health and Rehabilitation Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, PO Box 241, Cape Town 8000, South Africa (kberner@sun.ac.za).

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changes in movement quality and lower limb function in PWH. However, interpreting discrete and interdependent gait data is complex. Composite gait scores calculated from biomechanical variables, such as the Enhanced Gait Variability Index (EGVI), account for interdependence and provide more user-friendly index scores that quantify overall gait pattern deviation [8]. The EGVI quantifies gait variability, which has been associated with unstable walking and future mobility disability [9, 10]. It is unfortunate that 3DGA is not routinely available in many poorly resourced healthcare settings. The clinical measures with which it correlates may therefore offer useful alternative clinical screening tests for early functional decline in PWH. This information will inform early interventions to minimize future morbidity and healthcare utilization.

This study reports novel information about gait impairments in PWH captured by 3DGA. It explores associations between 3DGA, self-reported function, falls-related outcomes, and pragmatic physical performance tests applicable to clinical practice, with the aim of identifying a sensitive clinical screening test for early functional decline in PWH.

## METHODS

### Study Context

This paper reports on a cross-sectional substudy nested within a longitudinal cohort (Cape Winelands HAART to HEART Study).

### Ethics Approval and Patient Consent

The study protocol was approved by the Stellenbosch University Health Research Ethics Committee (N15/05/043) and the Western Cape Department of Health (WC\_2016RP10\_878). All participants provided written informed consent.

### Participants

The study compared PWH with HIV-seronegative participants (SNP). Two primary care community health centers with HIV clinics in the Cape Winelands, South Africa, provided participants. The study population was described previously in a related study using the same participants [11]. Research nurses or HIV-counselors consecutively recruited participants between June 2016 and December 2017. Participants included those (1) aged 18–65, (2) not overweight (body mass index [BMI] <25 kg/m<sup>2</sup>), (3) independently ambulant, and (4) able to consent. Exclusion criteria were (1) pregnancy, (2) acute infection/illness, (3) peripheral neuropathy, (4) major neurological conditions, (5) neuromusculoskeletal impairments/injury that affected gait, (6) visual impairment, and (7) alcohol intoxication. The eligibility criteria aimed to exclude factors substantially affecting usual gait or the quality of 3-dimensional (3D) data. We thus included a cohort without obvious predisposing factors to gait/balance impairments. For example, peripheral neuropathy and obesity may cause functional gait and balance impairments

and have been associated with falls in PWH [12–15]. Increased awareness of gait deviations within a population without obvious risk factors could contribute to more regular screening, which may be useful for reducing walking-related risks or injury severity. Furthermore, subcutaneous tissue movement is known to influence 3D data collected using body-worn inertial motion capture systems; this is less likely with lower BMI ranges [16].

Human immunodeficiency virus status was confirmed via rapid blood test. Participants provided written informed consent, including specific consent for HIV testing. Pre- and posttest counseling was available as needed.

### Sample Size

Sample size was based on gait biomechanics data from the first 30 substudy participants. Preliminary analysis identified the most variable gait angle as ankle dorsiflexion at initial contact. Using the pooled standard deviation (SD) for this angle (8.4), 5% significance and 80% power, a sample of at least 45/group was required to detect a 5-degree minimum clinically important difference [17]. To allow for missing data, a sample of  $n = 50$  per group was sought. Post hoc analysis determined that this sample had 83% power to detect a moderate correlation ( $r = 0.4$ ) between clinical tests and a composite gait score (EGVI).

### Three-Dimensional Gait Analysis

A wireless, portable inertial motion capture (IMC) system (myoMOTION Research Pro; Noraxon USA Inc.) was used to capture walking biomechanics (28 lower limb kinematics and 15 time-space parameters [TSPs] [18], which may be affected in elderly or fall-prone gait [19–24]). Seven inertial measurement units (IMUs) were placed on body segments according to a rigid lower body model provided by the system. The system was recalibrated before each walking trial [18] (see [Supplementary Material](#) for further detail).

### Composite Gait Score

The EGVI was used as a composite score to quantify gait pattern variability. The EGVI is based on 5 TSPs associated with functional outcomes and falls risk (step length, step time, stance time, single support time, and stride velocity) [25, 26] and quantifies the difference in variability between reference and patient groups [25]. A score of 100 indicates “normal” gait variability; higher and lower scores, respectively, indicate increased and decreased variability [25]. See the [Supplementary Material](#) for further detail.

### Dual Tasking

Dual tasking was introduced after protocol amendment, thus data were unavailable on early participants. Participants were required to perform some 3DGA, single leg stance (SLS), and

clinical walking trials while counting aloud backwards [27]—ie, demonstrate dual control of motor and cognitive functions (see [Supplementary Material](#)).

#### Physical Performance Tests

These included the 6-meter walk test (6mWT) [28], the 30-second SLS (eyes open and closed) [29], the 5-times sit-to-stand test (5STS), and the Health ABC Physical Performance Battery (PPB) [30]. The [Supplementary Material](#) provides details regarding these tests and their scoring. Because the 6mWT, 5STS, and SLS also form part of the PPB, these tests were scored in 2 ways: (1) as part of the PPB to obtain the overall battery score, and (2) as stand-alone clinical tests (eg, not converting the test times, speed, or repetitions to scores but using the raw values).

#### Self-Reported Outcomes (Function and Falls)

The EQ-5D-5L [31] is a standardized and concise health-related quality-of-life questionnaire that is suitable for use in PWH [32] and provides a profile of an individual's function and a global health state [33] (see [Supplementary Material](#) for further information). Three function-related dimensions of the EQ-5D-5L measured self-perceived function (mobility, self-care, and usual activities) [33]. Fall-related history included self-reported falls in the past 12 months (any/none), number of falls (single versus  $\geq 2$ ), and fear of falling ([FOF] yes/no) [11].

#### Other Variables

Most demographic, health, and lifestyle information were obtained by the broader longitudinal study using questionnaires, medical folders, and interviews (sex, education, employment, income, medication, chronic comorbidities, HIV and *antiretroviral therapy* [ART] history, smoking, self-reported physical activity, and alcohol consumption). Other measures obtained from the broader study included anthropometry and laboratory results for CD4 count and viral load (dichotomized at detectable threshold [ $\geq 50$  cp/mL]). Participants in the current substudy (1) completed a supplementary questionnaire to assess pain, cognition, depressive symptoms, and combination ART (cART) adherence (dichotomized as taking ART as prescribed all or most of the time, or not compliant) [34], (2) were screened for peripheral sensory neuropathy, and (3) underwent lower limb isometric strength testing [35]. The [Supplementary Material](#) provides further details.

#### Study Procedures

Data were collected at the 2 sites in quiet, hard-floored rooms. The study visit included questionnaire completion, physical measurements, 3DGA, and random-sequence functional test performance. To standardize the testing protocol and facilitate skin-attachment of IMUs, participants were barefoot and dressed comfortably. Practice trials for 3DGA were performed

after the IMUs were positioned, but before IMC calibration. For the 3DGA trials, conducted using standardized procedures, participants walked along a 10-meter walkway under 3 randomized conditions: (1) self-selected usual pace; (2) as fast as possible without running; and (3) with a DT. Participants performed 3 trials per condition. Walking started 1 meter before a line on the floor and ended after crossing a second line. A gait trial was deemed successful if 3 strides per limb were achieved.

#### Data Management

Inertial measurement unit data were transmitted wirelessly to a recording laptop and exported to MATLAB software (R2017a; MathWorks) for processing. Three successful 3DGA gait trials per condition were analyzed per participant. Cyclical gait events (foot contact and foot-off) were determined using a built-in algorithm in the software. This segmented the data into gait cycles normalized in time to 101 data points at 1%-time intervals. After gap-filtering, outcomes were (1) determined using analysis scripts and visualizations and (2) exported to MS Excel for analysis. The EGVI calculations were based on 5 TSPs generated within the 3DGA software, custom-formatted for use within the Excel EGVI macro [25]. Raw data were obtained from the 3 gait trials per participant. Within each trial, EGVI calculation was conducted if at least 3 consecutive values for each alternative parameter were available [36]. The macro calculates an overall EGVI score as a composite score around a z-score of 100, using the absolute difference between successive values of the same series (trial and leg) [25] (see [Supplementary Material](#) for further details).

#### Statistical Analyses

SPSS V25.0 (IBM Corporation, Armonk, NY) and STATA V14.2 (StataCorp 2015, Stata Statistical Software: Release 14; StataCorp, College Station, TX) were used. Statistical significance was set at  $P < .05$ . Data normality and homogeneity of variance for analyses of covariance (ANCOVA) were confirmed. Data were summarized, as relevant, using mean and SD, median and interquartile range, and frequencies and percentages. Floor and ceiling effects of  $>15\%$  were considered significant for those clinical tests with maximum and minimum cutoff scores [37]. For univariate analyses, differences between PWH and SNP were determined using independent  $t$  tests, Mann-Whitney  $U$  tests,  $\chi^2$  tests, or Fisher exact tests. Clinical tests and 3DGA data were compared between groups using factorial ANCOVA. For clinical tests, covariables were age, sex, leg length, anxiety-depressive symptoms, smoking status, and physical activity. For 3DGA, covariables included dimensionless (gravity- and leg-length-normalized) gait speed, age, and sex. Separate ANCOVA models were created for each dependent variable, treating clinical tests as continuous variables in all analyses [28]. Where significant interactions were noted between HIV-serostatus and the factors/

covariables included in the ANCOVA, an “HIV × covariable” term was included in the final model [38]. Nonsignificant interaction terms were serially removed from the model [38].

Correlations between clinical tests and EGVI scores, self-reported function, and fall history were evaluated using Spearman’s rank ( $r_s$ ) correlation coefficients and Pearson product-moment ( $r$ ) coefficients. Correlations of  $0.20 \leq 0.39$  were weak; correlations of  $0.40 \leq 0.59$  were moderate; correlations of  $0.60 \leq 0.79$  were strong; and correlations of  $0.80 \leq 1.00$  were very strong [39]. Associations between (1) clinical tests and (2) each falls variable were assessed using independent  $t$  tests or Mann-Whitney  $U$  tests.

## RESULTS

Of 186 participants screened, 106 were eligible, and after further exclusion, 50 PWH and 50 SNPs participated in all tests (Supplementary Figure 1). Dual-tasking data were collected for 41 of 50 PWH and 47 of 50 SNP. Due to insufficient detection of consecutive strides, usual-pace EGVI scores were calculated for 44 PWH and 29 SNP, DT EGVI for 26 PWH and 30 SNP, and fast EGVI for 0 participants.

### Participant Characteristics

There were significant differences between PWH and SNP regarding age, sex, leg length, muscle strength, physical activity, smoking, polypharmacy, anxiety-depression, self-reported function, and falls history (Table 1).

### Enhanced Gait Variability Index

For usual-paced gait, EGVI scores were significantly higher for PWH than SNP (age-sex adjusted MD = 14.7, standard error [SE] = 2.4, 95% confidence interval [CI] = 9.9–19.5,  $P < .001$ ). Under the DT condition, PWH obtained higher scores than SNP, but the difference was not statistically significant after age-sex adjustment (MD = 6.4, SE = 3.2, 95% CI = 0.1–12.8,  $P = .052$ ) (Figure 1).

### Three-Dimensional Gait Analysis Outcomes

Table 2 presents adjusted comparisons between PWH and SNP for TSP and joint angles (Supplementary Tables 1A and 1B present results per group and task-condition). For usual-paced gait, PWH walked slower with longer stance and step times. Human immunodeficiency virus-serostatus showed significant main effects only for gait speed ( $F = 15.8$ ,  $P < .001$ ). Significant interactions were noted between (1) HIV-serostatus and sex on stance time ( $F = 4.9$ ,  $P = .029$ ) and step time ( $F = 5.0$ ,  $P = .029$ ) and also between (2) HIV-serostatus and gait speed on stance time ( $F = 14.9$ ,  $P < .001$ ) and step time ( $F = 12.3$ ,  $P = .001$ ). For both stance time and step time, HIV effects appear larger in men and slower walkers. For fast gait, all differences were nonsignificant, except for step time (longer in PWH). Under DT conditions, gait speed was significantly slower in PWH,

with longer stride length and step time. A significant interaction existed for HIV-serostatus and gait speed on step time ( $F = 22.1$ ,  $P < .001$ ); the effects of HIV being more apparent at slower speeds.

For joint angles, significant differences existed only for DT walking. These differences occurred at the pelvis, hip, and knee at various points during the gait cycle. A significant interaction was noted between HIV-serostatus and gait speed on knee flexion *range of motion* (ROM). Under DT conditions, the effect of HIV on reducing knee flexion ROM depended on the walking speed and appeared larger at slower speeds.

### Clinical Test Performance

Table 3 summarizes differences in clinical test performance between PWH and SNP (Supplementary Table 2 presents results per group). Significant interactions existed between HIV-serostatus and anxiodepressive symptoms for both PPB gait speed subscores ( $F = 6.2$ ,  $P = .015$  and  $F = 4.9$ ,  $P = .029$  for usual and narrow tests, respectively). This suggested that the effect of HIV on gait speed scores depended on anxiodepressive symptoms (larger effect in the presence of symptoms). The PPB and its components demonstrated no significant floor or ceiling effects in either group, except for the balance score (highest level assessed: 30s SLS Eyes Open [EO]). Both groups demonstrated high ceiling effects for DT SLS. There were no between-group differences for SLS EO as part of the PPB subscore, and given the high ceiling effects, this test was not analyzed further as a stand-alone functional measure. A significant interaction existed between HIV-serostatus and anxiodepressive symptoms on usual-paced walking speed without DT ( $F = 5.5$ ,  $P = .021$ ). This interaction was similar for the PPB walking subscores. A significant interaction existed between HIV-serostatus and age on 5STS time ( $F = 6.1$ ,  $P = .016$ ), suggesting that the detrimental effect of HIV-serostatus on 5STS increases with age.

Correlations of clinical tests with the EGVI and self-reported outcomes in PWH Table 4 reports correlations of the clinical tests with the EGVI, self-reported function, and falls history for PWH. The 5STS correlated most strongly with EGVI scores, also showing moderate correlations with mobility function and self-care problems. People with HIV with slower 5STS demonstrated higher EGVI, as did those reporting functional problems (Supplementary Figure 2).

Associations between clinical tests and falls history are reported in Supplementary Table 3. People with HIV reporting FOF had poorer scores in total PPB ( $P = .008$ ), PPB narrow walk ( $P = .048$ ), and PPB chair rise ( $P = .008$ ). Those with FOF also performed more poorly in SLS Eyes Closed ( $P = .004$ ), had slower 5STS times ( $P = .003$ ), and fewer 30sSTS repetitions ( $P = .021$ ). The PPB balance subscore was the only test with a significant association with recent falls ( $P < .001$ ). The EGVI scores were not correlated to HIV duration or ART use (Supplementary Table 4).



**Table 1. Participant Characteristics**

Characteristic	PWH (n = 50)	SNP (n = 50)	P
Age, median (IQR)	36.6 (32.0– 45.6)	31.1 (23.2– 45.1)	<b>.017</b>
Younger than 50, n (%)	40/50 (80.0)	43/50 (86.0)	.424
Women, n (%)	29/50 (58.0)	40/50 (80.0)	<b>.017</b>
Education < Grade 12, n (%)	29/50 (58.0)	28/50 (56.0)	.840
Employed, n (%)	29/50 (58.0)	20/50 (40.0)	.072
Total monthly household income, n (%)			.645
<R1000	16/50 (32.0)	12 (24.0)	-
R1000–R4999	22/50 (44.0)	24 (48.0)	-
R5000–R9999	8/50 (16.0)	7/50 (14.0)	-
R10 000–R20 000	4/50 (8.0)	5/50 (10.0)	-
>R20 000	0/50 (0.0)	2/50 (4.0)	-
Height in meters, mean (SD)	1.6 (0.1)	1.6 (0.1)	.061
BMI, kg/m <sup>2</sup> , mean (SD)	21.5 (4.8)	20.4 (5.0)	.677
Leg length, cm, mean (SD)	86.8 (5.5)	84.5 (4.1)	<b>.016</b>
Muscle strength, Newton			
Plantarflexors, mean (SD)	169.2 (36.2)	181.9 (30.3)	.059
Dorsiflexors, mean (SD)	133.0 (23.9)	131.8 (23.6)	.798
Knee extensors, mean (SD)	189.1 (38.0)	203.8 (34.3)	<b>.045</b>
Knee flexors, mean (SD)	147.1 (32.6)	161.1 (26.6)	<b>.020</b>
Hip extensors, mean (SD)	216.9 (39.0)	212.2 (34.3)	.523
Hip flexors, mean (SD)	205.5 (37.3)	193.8 (28.2)	.078
Hip abductors, median (IQR)	103.6 (86.4–126.4)	109.2 (100.1–125.8)	.082
Physical activity, n (%) <sup>a</sup>			<b>.033</b>
None	6/50 (12.0)	15/50 (30.0)	-
Low	22/50 (44.0)	23/50 (46.0)	-
Moderate to high	22/50 (44.0)	12/50 (24.0)	-
Alcohol use over past 12 months, n (%)			.334
None	24/50 (48.0)	19/50 (38.0)	-
Light	18/50 (36.0)	27/50 (54.0)	-
Moderate	6/50 (12.0)	3/50 (6.0)	-
Heavy	2/50 (4.0)	1/50 (2.0)	-
Current smoker, n (%)	26/50 (52.0)	36/50 (72.0)	<b>.039</b>
Injection drug use, ever, n (%)	1/50 (2.0)	0/50 (0.0)	.500
Nonantiretroviral polypharmacy, n (%)	16/50 (32.0)	5/50 (10.0)	<b>&lt;.001</b>
Multimorbidity, n (%)	4/50 (8.0)	2/50 (4.0)	.678
Anxio-depressive symptoms, EQ-5D-5L, n (%)	12/48 (25.0)	2/50 (4.0)	<b>.003</b>
Pain, MOS-HIV score, median (IQR)	77.8 (55.6–88.9)	88.9 (77.8–100.0)	.127
Cognitive function, MOS-HIV score, median (IQR)	80.0 (60.0–95.0)	87.5 (75.0–95.0)	.076
Self-rep. function: EQ-5D-5L Mobility problems, n (%)	11/49 (22.5)	4/50 (8.0)	<b>.046</b>
Self-rep. function: EQ-5D-5L Self-care problems, n (%)	6/49 (12.2)	1/50 (2.0)	<b>.047</b>
Self-rep. function: EQ-5D-5L Usual activities, n (%)	10/49 (20.4)	4/50 (8.0)	.077
Any fall during past 12 months, n (%)	17/50 (34.0)	8/50 (16.0)	<b>.038</b>
Number of falls during past 12 months, n (%)			.114
Single	10/50 (20.0)	5/50 (10.0)	
Recurrent (2 or more)	7/50 (14.0)	3/50 (6.0)	
Fear of falling, n (%)	10/50 (20.0)	7/50 (14.0)	.425
Years since HIV diagnosis, n (%)			
<2	9/50 (18.0)	-	-
2<5	16/50 (32.0)	-	-
5–15	22/50 (44.0)	-	-
>15	3/50 (6.0)	-	-
Current CD4 <sup>+</sup> count, cells/μL, mean (SD)	448.8 (233.0)	-	-
Detectable viral load, ≥50 cp/mL, n (%)	25/46 (54.4)	-	-
On cART, n (%)	45/50 (90.0)	-	-
First-line cART, n (%)	38/45 (84.4)	-	-
Second-line cART, n (%)	7/45 (15.6)	-	-
cART duration in weeks, median (IQR)	119 (62–312)	-	-

**Table 1. Continued**

Characteristic	PWH (n = 50)	SNP (n = 50)	P
cART regime, n (%)			
PI-based	9/45 (20.0)	-	-
NNRTI-based	36/45 (80.0)	-	-
INI-based	0/45 (0.0)	-	-
cART adherent, n (%)	35/45 (77.8)	-	-

Abbreviations: BMI, body mass index; cART, combination antiretroviral therapy; HIV, human immunodeficiency virus; INI, integrase inhibitor; IQR, interquartile range; MOS-HIV, Medical Outcomes Study HIV Health Survey; NNRTI, nonnucleoside reverse-transcriptase inhibitor; PI, protease inhibitor; PWH, people with HIV; rep., report; SD, standard deviation; SNP, HIV-seronegative participants.

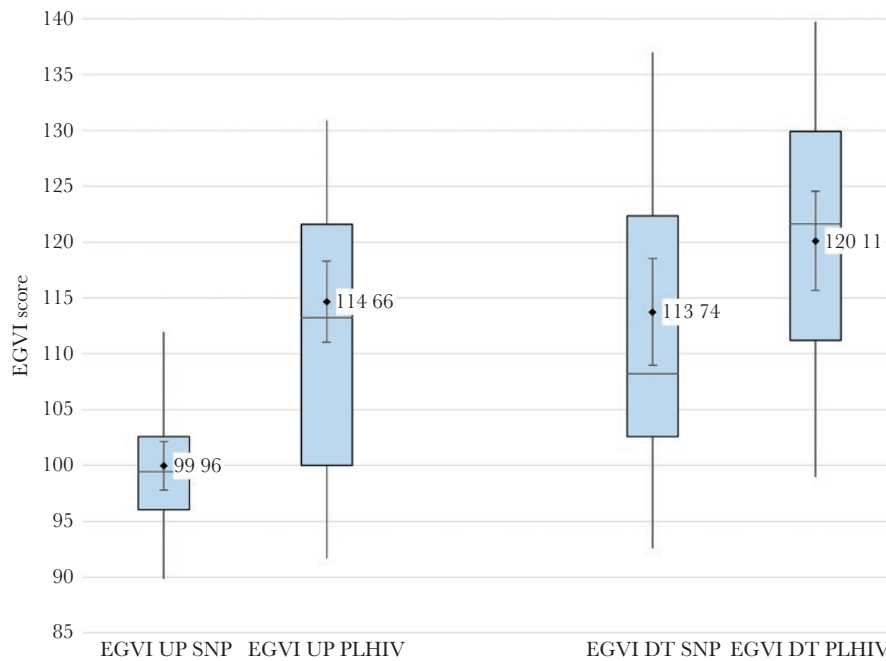
<sup>a</sup>Physical activity (PA) was based on self-report. Engaging in PA for <60 minutes/week (or <2 days/week) was deemed low PA. Engaging in mild to moderate exercise for >60 minutes/week, or participating in ≥30 minutes of moderate (or higher intensity) exercise for ≥5 days/week (or ≥150 minutes/week) were grouped together as moderate-to-high levels of PA [51]. Bold formatting indicates statistical significance at 5%.

**DISCUSSION**

This study is the first to describe biomechanical differences in the gait of PWH relative to HIV-free peers. Our findings further suggest the 5STS as a clinical test that might be relevant for early screening for gait deviations in PWH, given the correlations with increased gait variability and self-reported functional problems. Young-to-middle-aged PWH without obvious predisposing factors for mobility problems presented with a slowed and more variable gait pattern. The observed deviations were subtle, and had we included PWH with peripheral neuropathy, gait differences might perhaps have been even more pronounced. Chair stand performance was slower in PWH, and slowed 5STS performance in PWH was related to increased gait variability, worse self-reported function, and FOF. People with HIV walked with a significantly

more variable gait than SNP, which may be interpreted as unstable walking [9, 10]. Adopting a more variable gait may suggest impaired motor control (particularly implicating brain areas important for sensorimotor integration and coordination [40]). The associated foot placement errors and instability may be compounded in PWH by prolonged automated postural response latencies and abnormal postural reflex regulation [2]. People with HIV may thus have an increased falls risk when exposed to unexpected perturbations. Although there was no correlation between EGVI scores and recent falls events, the value of the EGVI in predicting falls warrants further investigations.

People with HIV gait demonstrated significant slowing, evidenced by increased time-related parameters such as absolute time spent in stance and producing steps. Because this remained



**Figure 1.** Enhanced Gait Variability Index (EGVI) scores in human immunodeficiency virus (HIV)-negative participants (SNP) and people with HIV (PWH) for usual-paced (UP) and dual-task (DT) walking. Plots show mean scores (labeled diamonds) with 95% confidence intervals (capped vertical error bars) as well as median scores (horizontal lines), score range (uncapped vertical error bars), and interquartile range (boxes).

Table 2. Differences in Biomechanical Outcomes for Usual-Paced (n PWH = 50, n SNP = 48), Fast (n PWH=45, n SNP = 45) and DT (n PWH = 39, n SNP = 47) Walking

Three-dimensional gait analysis outcome (time/space parameter or angle)	Usual-paced		Fast		Dual task	
	Adjusted MD (95% CI)	PWH vs SNP	Adjusted MD (95% CI)	PWH vs SNP	Adjusted MD (95% CI)	PWH vs SNP
Step length, cm	1.3 (-0.4 to 3.0)	↑	1.1 (-0.7 to 2.9)	↑	2.0 (-0.1 to 4.1)	↑
Normalized step length <sup>a</sup>	0.0 (-0.0 to 0.0)	↑	0.0 (-0.0 to 0.0)	↑	0.0 (-0.0 to 0.1)	↑
Stride length, cm	2.4 (-1.0 to 5.8)	↑	2.1 (-1.5 to 5.7)	↑	4.5 (0.3 to 8.8)	↑*
Normalized stride length <sup>b</sup>	0.0 (-0.0 to 0.1)	↑	0.0 (0.0 to 0.1)	↑	0.1 (-0.0 to 0.1)	↑
Cadence, steps/min	-2.1 (-4.6 to 0.5)	↓	-2.7 (-5.8 to 0.3)	↓	-3.8 (-7.6 to 0.0)	↓
Normalized cadence <sup>a</sup>	-0.5 (-1.2 to 0.2)	↓	-0.8 (-1.6 to 0.1)	↓	-1.1 (-2.2 to 0.1)	↓
Stance time, ms	20.0 (0.0 to 30.0)	↑*	10.0 (-0.0 to 30.0)	↑	20.0 (0.0 to 50.0)	↑
Step time, ms	20.0 (2.0 to 30.0)	↑*	10.0 (0.0 to 20.0)	↑*	190.0 (330.0 to 350.0) <sup>b</sup>	↑* <sup>b</sup>
Single support time, ms	10.0 (-0.0 to 30.0)	↑	10.0 (0.0 to 20.0)	↑	20.0 (0.0 to 40.0)	↑
Double support time, ms	0.0 (-10.0 to 20.0)	↑	10.0 (-10.0 to 20.0)	↑	10.0 (10.0 to 30.0)	↑
Stance percentage, %GC	-0.1 (-0.7 to 0.5)	↓	-0.1 (-0.6 to 0.5)	↓	-0.3 (-1.1 to 0.5)	↓
Single support percentage, %GC	0.2 (-0.5 to 1.0)	↑	0.1 (-0.6 to 0.7)	↑	-0.1 (0.8 to 0.7)	↓
Double support percentage, %GC	0.3 (-1.1 to 1.8)	↓	-0.1 (-1.1 to 0.9)	↓	-0.3 (-1.7 to 1.2)	↓
Gait speed, m/s <sup>b</sup>	-0.2 (-0.3 to -0.1)	↓*	-0.1 (-0.2 to 0.0)	↓	-0.2 (0.3 to -0.1)	↓*
Normalized gait speed <sup>b</sup>	<b>-0.1 (-0.1 to -0.0)</b>	↓*	-0.0 (-0.1 to 0.0)	↓	<b>-0.1 (-0.1 to -0.0)</b>	↓*
Pelvis tilt ROM, degrees	-0.3 (-1.4 to 0.7)	↓	0.3 (-0.8 to 1.5)	↑	0.1 (-0.9 to 1.1)	=
Peak pelvis anterior tilt, degrees	-0.2 (-2.0 to 1.7)	↓	0.0 (-1.7 to 1.8)	=	0.7 (-1.1 to 2.5)	↑
Pelvis obliquity ROM, degrees	-0.8 (-1.9 to 0.3)	↓	0.4 (-0.9 to 1.6)	↑	-0.5 (-1.7 to 0.7)	↓
Pelvis rotation ROM, degrees	0.5 (-1.2 to 2.3)	↑	1.6 (-0.2 to 3.4)	↑	1.3 (-1.1 to 3.6)	↑
Pelvis rotation at initial contact, degrees	0.2 (-1.2 to 1.5)	↑	0.8 (-0.7 to 2.4)	↑	<b>1.8 (0.3 to 3.3)</b>	↑*
Hip flexion ROM, degrees	0.9 (0.6 to 2.3)	↑	0.4 (-1.1 to 1.9)	↑	<b>2.4 (0.5 to 4.4)</b>	↑*
Hip flexion ROM during loading response, degrees	0.2 (-0.9 to 1.4)	↑	0.4 (-0.5 to 1.4)	↑	-0.4 (-1.6 to 0.8)	↓
Hip flexion ROM pre-swing; initial swing, degrees	0.2 (-1.0 to 1.4)	↑	-0.4 (-1.4 to 0.6)	↓	-0.0 (-1.2 to 1.1)	=
Hip flexion at initial contact, degrees	0.6 (-1.5 to 2.7)	↑	0.1 (-1.9 to 2.1)	=	<b>2.8 (0.6 to 4.9)</b>	↑*
Peak hip flexion during swing, degrees	0.00	=	-0.4 (-2.3 to 1.5)	↓	1.7 (-0.3 to 3.8)	↑
Peak hip extension during stance, degrees	1.1 (-0.6 to 2.9)	↑	1.1 (-1.4 to 3.6)	↑	0.6 (-1.5 to 2.7)	↑
Hip abduction ROM during mid-stance, degrees	-0.2 (-1.0 to 0.6)	↓	-0.2 (-1.1 to 0.8)	↓	0.7 (-0.1 to 1.5)	↑
Hip abduction ROM during loading response, degrees	-0.5 (-1.4 to 0.4)	↓	-0.3 (-1.2 to 0.6)	↓	-0.4 (-1.4 to 0.7)	↓
Hip internal rotation ROM, degrees	-0.7 (-2.5 to 1.2)	↓	0.1 (-1.7 to 1.9)	=	-0.0 (-2.3 to 2.3)	=
Knee flexion ROM, degrees	-0.6 (2.4 to 1.2)	↓	0.4 (-1.3 to 2.0)	↑	<b>-2.9 (-5.1 to -0.6)</b>	↓*
Knee flexion ROM during stance, degrees	-0.3 (-2.0 to 1.3)	↓	-0.7 (-2.3 to 0.8)	↓	0.8 (1.1 to 2.6)	↑
Knee flexion ROM from stance; swing, degrees	0.24 (-1.6 to 2.1)	↑	0.4 (-1.3 to 2.2)	↑	-2.3 (-4.6 to 0.0)	↓
Knee extension ROM from mid-stance; terminal stance, degrees	0.9 (-0.9 to 2.7)	↑	0.3 (1.6 to 2.2)	0.737↑	<b>2.3 (0.3 to 4.4)</b>	↑*
Knee flexion at initial contact, degrees	1.5 (-0.9 to 4.0)	↑	-0.1 (-2.6 to 2.4)	0.941↓	<b>3.7 (1.0 to 6.5)</b>	↑*

**Table 2. Continued**

Three-dimensional gait analysis outcome (time/space parameter or angle)	Usual-paced		Fast		Dual task	
	Adjusted MD (95% CI)	PWH vs SNP	Adjusted MD (95% CI)	PWH vs SNP	Adjusted MD (95% CI)	PWH vs SNP
Peak knee flexion during stance, degrees	0.2 (-2.2 to 2.7)	↑	-1.5 (-3.7 to 0.7)	0.169↓	0.1 (-2.8 to 3.0)	=
Peak knee extension during stance, degrees	-1.2 (-3.2 to 0.9)	↑	0.8 (-0.9 to 2.6)	0.357↓	<b>-3.2 (-5.5 to -0.9)</b>	↓*
Peak knee flexion during swing, degrees	0.4 (-1.9 to 2.7)	↑	-0.8 (-2.9 to 1.2)	0.426↓	0.1 (-2.7 to 2.9)	=
Ankle dorsiflexion ROM during stance, degrees	-0.9 (-2.3 to 0.5)	↓	-0.30 (-1.7 to 1.1)	0.664↓	-1.1 (-2.8 to 0.50)	↓
Ankle dorsiflexion ROM during swing, degrees	-1.5 (-3.7 to 0.6)	↓	-1.4 (-3.6 to 0.9)	0.238↓	-1.4 (-4.1 to 1.4)	↓
Ankle plantarflexion ROM, heel rise; toe-off (push off), degrees	-2.0 (-4.2 to 0.2)	↓	-1.3 (-3.5 to 0.8)	0.219↓	-1.9 (-4.6 to 0.9)	↓
Ankle dorsiflexion at initial contact, degrees	-0.1 (-1.5 to 1.2)	↑	-0.4 (-1.7 to 1.0)	0.569↑	0.8 (-0.8 to 2.5)	↓
Ankle plantarflexion at toe-off, degrees	-0.9 (-3.4 to 1.6)	↓	-0.2 (-2.7 to 2.3)	0.874↓	-0.8 (-3.9 to 2.2)	↓
Peak ankle plantarflexion, degrees	-1.5 (-4.0 to 1.0)	↓	-0.4 (-3.0 to 2.2)	0.748↓	-1.9 (-5.0 to 1.2)	↓

Arrows indicate the directional trend of the difference between PWH and SNP; asterisks indicate statistical significance at 5%.

Abbreviations: GC, gait cycle; MD, mean difference; ms, milliseconds; m/s, meters per seconds; PWH, people with HIV; ROM, range of motion; s, seconds; SNP, HIV-seronegative participants.

\*Since normalized parameters are already scaled to leg length, multivariable models included absolute gait speed.

<sup>b</sup>Gait speed (absolute and normalized) was only adjusted for sex and age in multivariable models.

<sup>c</sup>Standard error (SE) and associated CI were estimated with robust HC3 SE due to a significant Levene's test ( $P = .02$ ).

evident after controlling for covariables, HIV-related disease physiology may be indicated as a contributing factor (eg, white matter alterations [41]). Our study provides new information about speed impairments. A systematic review suggested that PWH demonstrate slowed speeds when having to walk fast, but not when walking at a usual pace [2]. However, most of the studies reporting differences used predicted norms from the literature for comparison. Because gait patterns strongly relate to context [42], between-group differences may not be reliable when comparing data from different populations. Using an HIV-free comparison group from the same community, we found that when walking fast, PWH overcame impairments noted for usual-paced or DT gait. However, we did not determine whether this required more effort (eg, whether maintaining such a pace for an extended period would be possible without fatigue). Further research should investigate how long such performance can be maintained, and whether falls risk increases due to PWH exceeding their capacity for safe walking. The possibility that PWH can tap into resources to walk fast with kinematics similar to SNP may imply that early gait impairments may be reversible; however, this requires further research.

Under DT conditions, PWH walked slower with an increased step time, but also with longer stride lengths. The longer strides in PWH may perhaps be explained by prioritization of the counting task over walking. This resembles an adaptation observed in older adults during dual tasking [44]. In contrast, in young healthy adults, stride characteristics usually remain unchanged because the DT cost does not represent a high cognitive load. Dual-task walking additionally revealed deviations in PWH's joint ROM in a kinematic pattern resembling the age-related biomechanical plasticity (ie, increased hip and decreased distal mechanical output when walking) often seen in older adults [24]. Biomechanical plasticity is likely related to changes in neural and musculoskeletal function [44], and the associated walking strategy involves a distal-to-proximal shift in muscle function and thus joint ROM [24]. The underlying mechanism in PWH may perhaps be similar, given the potential involvement of central neuromotor control [45].

The significantly poorer 5STS performance by PWH concurs with studies of middle-aged PWH (~40–50 years) in high-income settings [4, 46]. Dose-response relationships exist between (1) slowed 5STS and mortality [4] and (2) good performance and greater QOL [3]. The clinical importance of the 5STS is further supported by studies showing that half of PWH in their forties demonstrate impaired performance, one third may further decline over time, and a poor baseline score (average: 9.6 seconds) predicts falls [46].

To understand the moderate correlations between 5STS and 3DGA, the aspects of function that they measure must be considered. Gait biomechanics may be categorized under the body function domain on the International Classification of Functioning, Disability and Health [47], whereas the activity



**Table 3. Clinical Functional Test Performance Differences Between People With HIV and HIV-Negative Participants<sup>a</sup>**

Clinical Test	Adjusted MD (95% CI)	PWH vs SNP	Interpretation
Physical Performance Battery Score, Range 0–1			
Total score	−0.32 (−0.48 to −0.15)	↓*	Worse in PWH
Balance score	−0.95 (−1.94 to 0.04)	↓	Worse in PWH
Usual walk score	−0.09 (−0.14 to −0.05)	↓*	Worse in PWH
Narrow walk score	−0.16 (−0.26 to −0.07)	↓*	Worse in PWH
Chair rise score	−0.09 (−0.14 to −0.04)	↓*	Worse in PWH
Single-Leg Standing Test Time, Seconds			
Eyes closed	−6.0 (−9.9 to −2.1)	↓*	Shorter (worse) in PWH
Dual task <sup>b</sup>	−4.7 (−9.8 to 0.4)	↓	Shorter (worse) in PWH
6 m Walk Test Speed, m/s			
Usual-paced	−0.3 (−0.5 to −0.2)	↓*	Slower (worse) in PWH
Dual task <sup>b</sup>	−0.2 (−0.3 to −0.1)	↓*	Slower (worse) in PWH
Chair Rise Tests			
5× Sit-to-stand time, seconds	1.9 (1.0 to 2.9)	↑*	Slower (worse) in PWH
30 s Sit-to-stand, repetitions	−4.8 (−8.6 to −1.0)	↓*	Less (worse) in PWH

Abbreviations: HIV, human immunodeficiency virus; m, meter; MD, mean difference; m/s, meters per second; PWH, people with HIV; s, second; SNP, seronegative participants.

<sup>a</sup>Arrows indicate the direction of the difference between PWH and SNP; asterisks/bold print indicate statistical significance at 5%.

<sup>b</sup>No dual-task data collected for n = 3 SNP and n = 9 PWH.

domain better represents the chair-rise movement. However, body functions are inherently related to functional activities. It has been demonstrated that rapid force-relaxation, rather than muscle activation, is affected in the knee extensors of cART-managed PWH [48]. Studies in other populations have also suggested that impaired muscle power (more so than weakness) can influence functional mobility [49]. Although our 3DGA did not include kinetics to quantify muscle power, a hypothesis of impaired lower limb muscle power in PWH would provide a feasible link between the observations for 5STS performance and gait biomechanics. The increased variability in PWH's gait may indicate reduced dynamic stability and less accurate responses to perturbations. The 5STS requires rapid and coordinated

lower limb biomechanics and dynamic balance, thus one might expect to observe at least some correlation with gait variability. However, 5STS also represents a different movement sequence than that involved in walking, and both activities may be influenced by factors not measured in this study.

Slowed 5STS also significantly correlated with poorer self-reported function and FOF. Although not yet studied in PWH, FOF is a major and complex health problem in community-dwelling elderly and may present in those with and without previous falls [50]. Clinical tests associated with FOF may already be able to identify potential falls risk in PWH; however, sensitive falls-risk screening tests should be investigated in prospective longitudinal research.

**Table 4. Correlations Between Clinical Performance Tests, Enhanced Gait Variability Index, Self-Reported Function, and Fall Number in PWH**

PWH	EGVI UP	EGVI DT	Mobility Problems	Self-Care Problems	Usual Activity Problems	Fall No. in Past Year
PPB total score	<b>−0.4*</b>	<b>−0.6*</b>	<b>−0.5**</b>	<b>−0.4**</b>	<b>−0.4**</b>	0.0
PPB balance score	0.1	0.2	−0.3*	−0.3*	−0.1	<b>−0.5**</b>
PPB usual walk score	−0.3 <sup>a</sup>	−0.3 <sup>a</sup>	<b>−0.5**</b>	<b>−0.4**</b>	<b>−0.4**</b>	0.1
PPB narrow walk score	−0.3 <sup>a</sup>	−0.2 <sup>a</sup>	<b>−0.4**</b>	<b>−0.4**</b>	<b>−0.4**</b>	0.2
PPB chair-rise score	<b>−0.4**<sup>a</sup></b>	<b>−0.6**<sup>a</sup></b>	<b>−0.4**</b>	<b>−0.5**</b>	−0.3*	−0.2
6mWT speed	−0.3 <sup>a</sup>	−0.3 <sup>a</sup>	<b>−0.5**</b>	<b>−0.4**</b>	<b>−0.4**</b>	0.1
6mWT DT speed	−0.3 <sup>a</sup>	<b>−0.5<sup>a</sup></b>	<b>−0.4*</b>	−0.1	−0.2	−0.1
5STS time	<b>0.5**<sup>a</sup></b>	<b>0.6**<sup>a</sup></b>	<b>0.4**</b>	<b>0.5**</b>	0.3*	0.2
5STS pace (stands/second)	<b>−0.5**<sup>a</sup></b>	<b>−0.6**<sup>a</sup></b>	<b>−0.4**</b>	<b>−0.5**</b>	−0.3*	−0.2
30sSTS repetitions	<b>−0.4**<sup>a</sup></b>	<b>−0.5**<sup>a</sup></b>	<b>−0.4*</b>	<b>−0.5**</b>	<b>−0.4**</b>	−0.1
30sSTS pace (stands/second)	<b>−0.5**<sup>a</sup></b>	<b>−0.5**<sup>a</sup></b>	<b>−0.4*</b>	<b>−0.5**</b>	<b>−0.4**</b>	−0.1
SLS EC time	−0.2	−0.0	<b>−0.5**</b>	<b>−0.5**</b>	−0.3*	−0.2
SLS DT time	0.1	0.2	0.0	−0.1	−0.3	−0.2

Abbreviations: 30sSTS, 30-Second Sit-To-Stand Test; 5STS, Five-times Sit-To-Stand Test; 6mWT, Six-meter Walk Test; DT, dual-task; EC, Eyes Closed; EGVI, Enhanced Gait Variability Index; PWH, people with HIV; PPB, Health ABC Physical Performance Battery; SLS, Single Leg Stance Test; UP, usual-paced.

<sup>a</sup>Pearson product-moment correlation (all other: Spearman rank-order correlation).

\*, Correlation is significant at the 5% level (2-tailed). Bold formatting indicates correlations ≥0.4 (moderate) or ≥0.6 (strong).

\*\* , Correlation is significant at the 1% level (2-tailed).

## Limitations

The cross-sectional design cannot infer causality. The study provides insights into young-to-middle-aged South African PWH without peripheral neuropathy or obesity, drawn from 2 clinical settings, compared with community-matched SNP. The results are not necessarily generalizable to other populations. Although we excluded individuals with pathologies such as neuropathy and injuries that may affect gait, we did not exclude other comorbidities that can affect gait, such as chronic pain. The magnitude of angular differences between-groups was small. However, the differences all exceeded measurement errors of the 3DGA system [18]. The EGVI calculation requires a minimum of 5 absolute differences [8, 25], which necessitated the exclusion of some datasets. Furthermore, this study used a limited number of steps, ie, the absolute minimum required for calculating the EGVI, due to the available space for 3DGA in the clinical settings. More steps will likely provide more robust results.

## CONCLUSIONS

In this South African rural sample, relatively young PWH presented with biomechanical walking deviations suggestive of a slowed and unstable gait pattern, especially under cognitive challenges. Apart from improving understanding of gait patterns in PWH, findings also underscore the need for early screening of PWH for motor impairments. Five-times STS may be useful to predict gait deviations in PWH. Further research is needed to determine whether the 5STS test predicts falls and whether the impairments noted in PWH are reversible.

## Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases online*. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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