Dual Roles of Fitness and Fatigability in the Life Space Mobility of Older Adults

by

Kyle D. Moored, PhD

BS, University of Michigan, 2014

PhD, Johns Hopkins University, 2020

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This thesis was presented

by

Kyle D. Moored, PhD

It was defended on

April 7, 2022

and approved by

Thesis Chair:
Nancy W. Glynn, PhD
Associate Professor, Department of Epidemiology
School of Public Health, University of Pittsburgh

Thesis Committee:
Andrea L. Rosso, PhD, MPH
Associate Professor, Department of Epidemiology
School of Public Health, University of Pittsburgh

Frederico G. S. Toledo, MD
Associate Professor, Department of Medicine
School of Medicine, University of Pittsburgh
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Kyle D. Moored, MS

University of Pittsburgh, 2022

Background: Cardiorespiratory fitness and fatigability are interrelated components of physical capacity that may jointly facilitate movement within one’s living environment (life-space mobility). We examined whether fitness and perceived fatigability, and the interaction between them, were associated with life-space mobility in a well-characterized cohort of older adults. Methods: Participants were from the preliminary data release of the Study of Muscle, Mobility, and Aging (SOMMA) baseline cohort (N=387, M_age=76.4±5.0, 57% women). Life Space Assessment scores (range: 0-120) incorporated level, frequency, and assistance used for life-space mobility (Mean=82.7±18.8). Fitness was measured as VO2peak (Mean=19.5±4.2 mL/kg/min) from symptom-limited treadmill testing. Fatigability cut-points included: 1) Borg Rating of Perceived Exertion (RPE) ≥10 after a steady-state treadmill test, 2) the Pittsburgh Fatigability Scale (PFS) Physical ≥15, and 3) PFS Mental ≥13. Linear regressions were adjusted for demographic, lifestyle, and health confounders. Results: The relationship between fitness and life-space mobility was nonlinear, where those within the lower range of fitness scores (VO2peak≤18) had 2.2-point greater life-space scores per 1-mL/kg/min greater VO2peak (95% CI: 0.68, 3.67, p=.005). The association was not significant for the upper range of fitness scores (VO2peak>18). Participants with higher fatigability on all measures (RPE≥10, PFS Physical≥15, PFS Mental≥13) had a 7.6-point lower mean life-space score (95% CI: -13.84, -1.34) after adjusting for demographics, but this was not significant after further adjusting for lifestyle and health factors. There was potential moderation of the fitness-life-space relationship by
fatigability, where associations within the lower fitness range (VO₂peak ≤ 18) were only significant for those with RPE ≥ 10 (B = 3.3, 95% CI: 1.06, 5.53, p-interaction = .078). **Conclusion:** Fitness may primarily limit life-space mobility if it falls below a critical threshold, where older individuals may need to operate closer to their maximum aerobic capacity to traverse their daily environments. Higher fatigability may moderate this relationship, as those with both low fitness and high fatigability had the lowest life-space scores. Public health interventions that target this high-risk group may mitigate further functional declines resulting from life-space constriction.
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Preface

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1.0 INTRODUCTION

The overarching goal of this study was to examine associations between life-space mobility and two important measures of capacity: cardiorespiratory fitness and perceived fatigability. Establishing potential risk factors for life-space mobility is critical, given how it is associated with several functional\textsuperscript{1,2} and psychosocial\textsuperscript{3,4} outcomes in later life. Furthermore, the number of homebound older adults in the U.S. has more than doubled in the past decade,\textsuperscript{5} in part due to the ongoing SARS-CoV-2 pandemic, making life-space mobility an timely and important public health issue for older populations.

1.1 Life-Space Mobility

Life-space mobility is defined as the spatial extent with which an individual typically travels within their larger environment.\textsuperscript{6,7} Life-space mobility is typically conceptualized as a series of concentric circles (i.e., “life-space levels”) centered on one’s bedroom and radiating out to include broader areas of their environment, including their home, yard, neighborhood, town, and beyond (see Figure 1 in Peel et al., 2005).\textsuperscript{7} Individuals who can access broader reaches of their environment are said to have greater life-space mobility. Unlike other activity measures (e.g., step activity, self-reported exercise), life-space mobility includes both active (e.g., walking) and passive (e.g., driving, taking transportation) travel. Life-space mobility is thought to better reflect the everyday mobility of older adults compared to clinical walking tests by incorporating both their internal physical capacity and external environment.\textsuperscript{7} This distinction is important, as measures of
enacted functioning, like life-space mobility, may sometimes be discordant with clinical mobility measures (i.e., experimental functioning) and represent distinct functional constructs relevant to health in later life (i.e., what somebody can do versus what they actually do).\textsuperscript{8}

Life-space mobility has been shown to be a key indicator of functional health and well-being in later life. Restrictions in life-space have been associated with mortality,\textsuperscript{2} incident frailty,\textsuperscript{1} and are thought to precede impairments with instrumental activities of daily living.\textsuperscript{6} Greater social engagement,\textsuperscript{4} greater social support,\textsuperscript{3} and fewer depressive symptoms\textsuperscript{9} are each associated with greater life-space mobility. Given the relationship of both incident physical impairments and psychosocial wellness with life-space mobility, examining modifiable risk factors of life-space constriction may be important for preserving holistic functioning later in life.

1.2 Factors Influencing Life-Space Mobility

Webber et al. provided a holistic framework that considers multiple intrinsic and extrinsic determinants of mobility.\textsuperscript{10} Based on a critical review of the literature, they identified five categories of determinants: 1) physical, 2) cognitive, 3) psychosocial, 4) environmental, and 5) financial. Although not explicitly mentioned, physical factors may include lower-extremity mobility, gait, and fitness (see Section 2.0).\textsuperscript{3,11} Cognitive factors may include memory, processing speed, and executive functioning; of which are important for spatial navigation and driving ability.\textsuperscript{12} Psychosocial factors may include self-efficacy, mental health, and social connections shown to be important to motivating activity.\textsuperscript{3,4} Environmental factors may include neighborhood location/resources and access to transportation.\textsuperscript{13} Finally, financial factors may include socioeconomic status, income, and wealth.\textsuperscript{14}
There are several nuances to this framework. First, the authors argue that these domains likely interact with one another. For example, financial factors such as income may contribute to environmental differences, such as access to transportation and neighborhood location, that further influence mobility. The five categories of determinants are also influenced by cross-cutting gender, cultural, and biographical differences. For example, women have been shown to have higher prevalence of mobility limitations compared to men. Culture may further impact mobility by affecting educational/occupational opportunities as well as behavioral factors (social relationships, physical activity). Finally, the authors depict their framework as an inverted conical structure (see Figure 1 in Webber et al.), where increased distance from home is represented by larger portions of the cone. This illustrates how the number of determinants and their associations with mobility likely become larger as one moves farther away from home.

In the current study, we used the Webber et al. model as a guiding conceptual framework to understand how objective fitness (physical factor) and perceived fatigability (physical/psychosocial factor) influence life-space mobility and how this relationship may be confounded by other cognitive, environmental, psychosocial, and financial factors. We included covariates in our analyses from each category delineated in the Webber et al. framework to encompass these comprehensive factors.
2.0 CARDIORESPIRATORY FITNESS

Cardiorespiratory fitness (i.e., aerobic capacity) encompasses the body’s ability to transport and utilize oxygen during maximal exercise.\textsuperscript{16,17} Gold-standard measures of fitness involve assessing changes in volume of oxygen consumption (\textit{VO}_2) during a progressive exercise test. \textit{VO}_2\text{max} is defined as the point at which oxygen uptake no longer increases with increased task demand.\textsuperscript{16} Unfortunately, \textit{VO}_2\text{max} can only be assessed if an individual reaches a plateau in oxygen consumption during testing (i.e., maximal versus submaximal exercise). As an alternative, \textit{VO}_2\text{peak} is defined as the maximum oxygen consumption achieved during exercise testing regardless of whether the individual reaches a plateau.\textsuperscript{16} Given that many older adults with chronic conditions cannot achieve maximal effort in a progressive exercise test, \textit{VO}_2\text{peak} may be preferred for this population.\textsuperscript{16,17} We used \textit{VO}_2\text{peak} as a measure of fitness in the current study, operationalized as the highest oxygen consumption averaged over 30-second intervals of symptom-limited exercise testing.

2.1 Exercise Testing Protocols

One challenge of comparing fitness estimates across older adult samples is the substantial variation in exercise testing protocols across studies. Progressive exercise testing is typically performed using either a treadmill or exercise bike. Most exercise testing in older adults is done using the treadmill, given the familiarity with walking compared to biking in this population.\textsuperscript{17} Further, studies have found that \textit{VO}_2\text{max} estimates were lower in bicycle testing compared to
treadmill testing, a discrepancy that may be further increased in older populations. Yet, using a bicycle versus a treadmill for exercise testing in older populations may mitigate safety concerns with balance.

In addition to differences in equipment, there is also variation between studies in how the progressive exercise is performed. Many studies of older adults use variations on the Bruce (1971) or Balke and Ware (1959) protocols. The Bruce protocol increments grade and speed in timed stages, whereas the Balke and Ware protocol uses a constant walking speed with a percentage increase in grade every minute. For older adults, there is large variation between studies in how speed and grade increment across the task. For example, Katzel et al., (2001) assessed VO\textsubscript{2}\text{max} used a modified Balke protocol where the initial speed was set to induce 70% of the individual’s peak heart rate based on an initial screening test, and then grade was increased by 2% per minute until the participant met the VO\textsubscript{2}\text{max} criteria or reported exhaustion. In contrast, Morey et al. (1998) assessed VO\textsubscript{2}\text{peak} using symptom-limited testing, where speed and grade were increased in 4-minute stages that were standardized across participants. The substantial variation in exercise testing methodology necessitates transparent and detailed reporting of protocols, which is often not done in studies of older adults.

2.2 Fitness as a Prognostic Health Indicator

Despite measurement variation, fitness has been found to be a key marker of physiologic aging. Fitness declines about 8-10% per decade across the adult lifespan and declines accelerate with increasing age. These changes may be mediated by accumulating cardiac (e.g., reduced cardiac output) and noncardiac (e.g., obesity, arthritis, etc.) conditions. Age-associated declines
in fitness are important because they further predict incident health outcomes. Higher VO$_2$peak was associated with lower risk of coronary death in both men with (28% per 1-MET increase) and without (12% per 1-MET increase) significant health conditions. In a large, population-based sample, a 1-MET increase in VO$_2$peak was further associated with a 15% reduced risk of coronary heart disease (CHD) across both sexes. Further, individuals in the highest VO$_2$peak quartile had a 48% lower risk of CHD compared to those in the lowest quartile. Finally, fitness has also been shown to predict mortality. In the Copenhagen Male Study, each 1-mL/kg/min increase in VO$_2$max measured at mid-life was associated with a 45-day increase in life expectancy. Compared to those in the lower half of normalized VO$_2$max scores, those in the upper half had a 2.9-year longer average life expectancy. Finally, the Social Security Administration has used a functional cut-point of 18 mL/kg/min to distinguish older adults with higher versus lower fitness. Despite no clear threshold effect in their data, decision tree analyses from Morey et al., (1998) showed that this cut-point for treadmill VO$_2$peak measures functionally distinguished older adults, and similar cut-points have supported in studies using VO$_2$max and exercise cycle VO$_2$peak measures. Although lower fitness is an important predictor of distal health events, it is currently unknown whether lower fitness may increase risk of these health conditions in part through impacting life-space mobility. One goal of the current work was to examine novel associations between gold-standard fitness (VO$_2$peak) and life-space mobility in a community-dwelling sample of older adults.
3.0 FATIGUE AND PERCEIVED FATIGABILITY

Fatigue is defined as the subjective lack of physical or mental energy that interferes with usual activities.\(^29,30\) Fatigue depends in part on the intensity and duration of the activity, as well as one’s current level of physical functioning. As a result, it is difficult to compare fatigue estimates across samples that vary in functional health and activity levels.\(^30\) Self-reported fatigue measures are further influenced by self-pacing bias,\(^29\) where individuals of poorer functional health may reduce the intensity which they complete activities to maintain tolerable levels of fatigue.

To address these issues, the field has moved to using measures of fatigability. Fatigability is defined as vulnerability to fatigue\(^29\) and is typically operationalized by anchoring fatigue measures to standardized activities.\(^30\) Fatigability can be further subdivided into performance fatigability and perceived fatigability. Performance fatigability is defined as an objective decrement in performance during a standardized physical task (e.g., fast-paced 400m walk). In contrast, perceived fatigability includes self-reported whole-body or cognitive fatigue standardized to activities of fixed intensity and duration.\(^29,31-34\)

3.1 Perceived Fatigability as a Prognostic Health Indicator

Perceived fatigability is the focus of the current study. Importantly, perceived fatigability minimizes self-pacing bias and facilitates comparison of fatigue estimates across samples with different functional health.\(^29,30\) Perceived fatigability has been shown to be a more sensitive
measure of functional declines and clinical outcomes than traditional fatigue measures \(^{31,34-37}\) and is therefore a key marker of physiologic aging.\(^ {30}\)

Perceived fatigability is also commonly reported by older adults.\(^ {38}\) In the Long Life Family Study, 25-90\% of adults aged 60-108 were estimated to have more severe perceived fatigability (Pittsburgh Fatigability Scale Physical ≥15).\(^ {39}\) The prevalence increased with age and was higher in women and individuals with poorer functional health. Higher perceived fatigability was also associated with greater all-cause mortality.\(^ {40}\) Taken together, perceived fatigability is a prevalent condition and important precursor on the disablement pathway in later life.

### 3.2 Connections between Fatigability, Fitness, and Physical Activity

In their summary of the fifth Bench-to-Bedside conference on “Idiopathic Fatigue and Aging”, Alexander et al. present a conceptual model for how fitness, fatigue, and physical activity changes may occur in a vicious cycle (Figure 1).\(^ {38}\) They posit that individuals with lower fitness (e.g., VO\(_2\)peak) may have poorer energy utilization or less total energy available to engage in physical activity, resulting in increased fatigue from activity of a set duration and intensity. Individuals likely adapt to this fatigue by reducing their activity levels (i.e., self-pacing), which in turn further reduces their fitness (e.g., from lack of exercise) and begins the cycle again. Declines in physical activity have been shown to precede changes in perceived fatigability in statistical mediation models,\(^ {41}\) suggesting that initial declines in activity may precipitate this process.

It is currently unclear where life-space mobility fits into this conceptual model, but we posit that severe life-space constriction (e.g., becoming homebound) is a downstream outcome resulting from repeated cycles of declines in fitness and increases in fatigability (Figure 1).
Although we previously found that perceived fatigability was correlated with life-space mobility in older men, no studies to-date have examined fitness and fatigability together as dual contributors to life-space mobility. Establishing correlational links between life-space mobility and both fitness and fatigability is an important first step to ultimately determining how life-space mobility fits into the larger disablement cycle.

Fitness and fatigability may further interact in their contributions to life-space mobility. Higher fatigability in combination with lower fitness may signal that an individual is farther along in the disablement pathway. Further, perceived fatigability may capture mental processes (e.g., perceived capacity to meet task demands) that may moderate the degree to which objective fitness impacts life-space mobility. Observing significant interactions between fitness and fatigability in their relationship with life-space mobility may reveal who is most at risk for life-space constriction. It may further suggest that interventions to mitigate life-space constriction need to target both factors simultaneously, a hypothesis that could be investigated in future longitudinal studies.
Figure 1: Vicious Cycle of Fitness and Fatigue on Life-Space Mobility

Note. This figure was adapted from the conceptual framework provided in Alexander et al. (2010). Declines in physical activity may precipitate declines in fitness. Lower fitness then reduces energy available to complete tasks, increasing fatigue. Individuals may adapt to increased fatigue by further reducing their activity, beginning the cycle again. Incident life-space constriction may be a downstream outcome of this vicious cycle that further contributes to distal health outcomes (social isolation, functional limitations, mortality).
4.0 GAPS IN KNOWLEDGE

There are several gaps in knowledge regarding functional contributors to life-space mobility. While physical performance has been shown to predict life-space mobility, these findings are largely limited to measures of walking speed. To our knowledge, no studies have examined associations between gold-standard measures of cardiorespiratory fitness (e.g., VO$_2$peak) and life-space mobility, despite fitness being an independent component of physical performance and key predictor of functional impairment and mortality. Examining the cross-sectional relationship between VO$_2$peak and life-space scores could provide initial evidence for an intermediatory role of life-space mobility in the larger pathway from fitness to disability and mortality.

Declines in fitness may further lead to life-space constriction through increased fatigue. Prior work from our group in the Osteoporotic Fractures in Men Study (MrOS) has found that life-space mobility is associated with perceived fatigability. However, the mechanism driving this relationship remains unclear, as our analysis was limited to one measure of perceived fatigability (Pittsburgh Fatigability Scale) and lacked gold-standard measures of fitness. Fitness contributes to the total energy available to engage in physical activity after accounting for regulatory processes (e.g., homeostasis, food absorption, thermogenesis). Lower fitness may therefore lower the threshold for fatigue in response to the same level of activity needed to maintain life-space mobility. Yet, fatigue is also inherently subjective, and fatigability measures may be further influenced by perceived task demands. Disentangling these mechanisms necessitates the use of both objective fitness (i.e., VO$_2$peak) and perceived fatigability measures (i.e., Ratings of Perceived Exertion (RPE), Pittsburgh Fatigability Scale (PFS)).
5.0 OBJECTIVES

The objectives of this study were to 1) examine cross-sectional associations between cardiorespiratory fitness, perceived fatigability, and life-space mobility, and 2) examine whether perceived fatigability modifies the association between fitness and life-space mobility. We hypothesized that both higher fitness and lower fatigability would be associated with higher life-space mobility. We further hypothesized that associations between fitness and life-space mobility will be greater in magnitude for individuals with higher perceived fatigability, highlighting the synergistic effect of objective and perceived capacity in determining the everyday mobility of older adults.
6.0 PUBLIC HEALTH RELEVANCE

Life-space mobility is a critical and relevant public health target. Due in part to the ongoing SARS-CoV-2 pandemic, the prevalence of homebound older adults in the U.S. more than doubled from 5% in 2011 to 13% in 2020,\(^5\) and the long-term impact of the pandemic on the life-space of older adults is currently unknown. Given its links with both incident functional impairments\(^1,6,7\) and psychosocial wellness,\(^3,4\) this increase in prevalence is not trivial, and examining modifiable risk factors for life-space constriction is crucial for preserving holistic functioning for older adults going forward.
7.0 METHODS

7.1 Participants

Participants came from the Study of Muscle, Mobility, and Aging (SOMMA), a prospective cohort study of mobility in community-dwelling older adults. The current study uses the initial data release for the baseline cohort, occurring between April 2019 and April 2021. SOMMA was conducted at two clinical sites: University of Pittsburgh (Pittsburgh, PA) and Wake Forest University (Winston-Salem, NC). Eligible participants were ≥70 years old at enrollment, had a body mass index (BMI) of 18-40 kg/m, and were eligible for magnetic resonance (MR) imaging and a muscle tissue biopsy. Participants also had to complete the usual pace 400-meter walk within 15 minutes and the 4-meter walk with a speed of at least 0.6 m/s.

SOMMA plans to enroll 875 participants for the baseline visit. The sample for the current data release consisted of 468 participants who completed all three days of baseline testing. Day 1 included general clinic assessments, Day 2 included MR imaging and Cardiopulmonary Exercise Testing (CPET), and Day 3 included fasting specimen and tissue collection. Seventy-one participants were excluded due to missing fitness or fatigability measures (Figure 1). Most missing fitness or fatigability measures were due to missing CPET measures (e.g., disqualified, did not perform). An additional 10 were excluded due to missing covariate measures, resulting in an analytic sample of 387 individuals.
Figure 2: Participants Included in Analyses

Note. CPET = Cardiopulmonary Exercise Testing, SS = steady-state phase, PWS = preferred-walking speed phase, RPE = Borg Rating of Perceived Exertion, PFS = Pittsburgh Fatigability Scale, LSA = Life Space Assessment

7.2 Cardiopulmonary Exercise Testing (CPET) Protocol

The treadmill CPET including three phases of testing administered by trained study personnel during Day 2 of baseline assessments. Blood pressure and heart rate were continually assessed during each phase to monitor participant safety. In Phase 1 (Preferred Walking Speed), participants walked at their preferred speed and 0% incline for five minutes to assess walking efficiency. Phase 2 (Symptom-Limited Peak) occurred immediately after Phase 1 and consisted of progressive exercise stimulation using a modified Balke protocol, with strong encouragement to reach a respiratory exchange ratio (RER) ≥ 1.05 and Borg Rating of Perceived Exertion
(RPE)≥15. Treadmill speed and incline were increased incrementally until the participant reported volitional exhaustion. After Phase 2, participants had a 20-minute rest period before starting Phase 3. In Phase 3 (Steady-State), participants walked at a speed of 0.67 m/s (1.5 mi/hr) and 0% incline for five minutes to assess fatigability (see Measures below).

Thirteen participants were only cleared for CPET Phases 1 (Preferred Walking Speed) and 3 (Steady-State) due to health and safety concerns, and 3 were cleared for but unable to perform Phase 2 (Symptom-Limited Peak) (Figure 1). Thirty-six individuals who completed Phase 2 were also excluded due to having invalid data based on the following criteria: 1) VO₂peak<12 mL/kg/min (n=22), 2) maximum RER<1.05 and maximum RPE<15 (n=3), and maximum heart rate <100 bpm.

7.3 Measures

7.3.1 Cardiorespiratory Fitness (VO₂peak)

Fitness was a primary exposure in the current study and was measured using gold-standard VO₂peak (mL/kg/min) from CPET. VO₂peak was quantified as the highest volume of oxygen consumption averaged over 30-second intervals of Phase 2 (Symptom-Limited Peak) testing. VO₂peak was calculated using BreezeSuite metabolic cart software (MGC Diagnostics, Saint Paul, MN) and adjusted for participant weight.
7.3.2 Perceived Fatigability

The current study included two primary measures of perceived fatigability (Figure 3): 1) Steady-state Rating of Perceived Exertion and 2) Pittsburgh Fatigability Scale.

7.3.2.1 Steady-State Rating of Perceived Exertion (RPE)

Participants rated their perceived exertion after a 5-minute steady-state treadmill task (CPET Phase 3).\textsuperscript{47,48} Scores ranged from 6 (very, very light) to 20 (maximum exertion), with higher scores indicating greater perceived physical fatigability in response to a fixed, light-intensity treadmill task. An established cutoff of ≥10 was used to identify participants with higher RPE fatigability.\textsuperscript{30}

7.3.2.2 Pittsburgh Fatigability Scale (PFS)

The PFS is a validated 10-item scale to assess perceived physical and mental fatigability.\textsuperscript{32,33} Participants reported physical and mental fatigue (0 = “no fatigue” to 5 = “extreme fatigue”) they expected or imagined they would feel after performing activities of fixed intensity and duration (e.g., “brisk or fast walk for 1 hour”). Sums of responses were used to generate physical and mental fatigability subscale scores (range: 0-50, higher PFS scores=greater fatigability). In contrast to RPE, PFS scores indicated perceived fatigability for a range of imagined tasks, rather than a fixed, light-intensity treadmill task. Established thresholds were used to identify participants with more severe physical (PFS≥15) and mental (PFS≥13) fatigability.\textsuperscript{30,34,49} Scores for 5 participants with missing data for 1-3 PFS items were imputed following an existing protocol.\textsuperscript{50} Scores were imputed using the mean of the individual’s valid responses, accounting for
sample-specific fatigue associated with the activity and whether participants performed the activity.

To utilize information from all three measures, we also created a fatigability composite indicator for participants meeting the thresholds for more severe fatigability on each measure (RPE≥10, PFS Physical≥15, PFS Mental≥13) (Figure 3). This was done in attempt to identify participants with the most severe fatigability, who may be at the highest risk of life-space constriction.

Figure 3: Overlap in Measures of Perceived Fatigability

Note. Cut-points for more severe fatigability are presented above for each measure included in the study (RPE≥10, PFS Physical≥15, PFS Mental≥13). A combined fatigability measure was created indicating participants who met each severity cut-point (i.e., center of the overlapping circles).
7.3.3 Life-Space Assessment

The primary outcome of life-space mobility was measured using the validated University of Alabama at Birmingham Life Space Assessment (LSA).\textsuperscript{6,7} Participants reported whether they traveled to each level of their life-space (e.g., beyond bedroom (1), home (2), yard (3), neighborhood (4), and/or town (5)) in the past 4 weeks. They also reported the frequency with which they traveled to each level (1=“<once/week to 4=“daily”) and whether they required assistance (1=“personal assistance,” 1.5=“equipment only,” and 2=“no equipment or personal assistance”). Life-space scores were computed by multiplying the level number, frequency, and assistance for that level, and then summing the five levels together (range: 0-120; higher score = higher life-space mobility).\textsuperscript{7} We also generated a binary indicator of whether the individual could not leave their neighborhood or town without assistance, which is indicative of life-space constriction.\textsuperscript{1}

Life-space mobility includes both active (e.g., walking) and passive (e.g., driving) transit, and driving status has been shown to be strongly associated with life-space mobility scores.\textsuperscript{3} Therefore, sensitivity analyses were performed excluding individuals who reported any difficulty driving or not being able to drive (n=12, 3%).

7.3.4 Covariates

Several known or potential demographic, social, lifestyle, and health confounders were included as covariates in analyses.\textsuperscript{10}
7.3.4.1 Demographics

Age at enrollment, gender, study site (Wake Forest vs. Pittsburgh), race, and education level were all recorded at baseline. Forty-four percent (n=170) of the analytic sample had their first baseline assessment (Day 1) on or after March 16, 2020, approximately the start of the COVID-19 pandemic quarantine period in the United States. The life-space mobility of older adults has substantially decreased since the start of the COVID-19 pandemic.\(^5\),\(^5\) We therefore included an indicator of whether the visit occurred on or after March 16, 2020 as a covariate in analyses. A small proportion of individuals (n=28, 8%) also had their three baseline assessments interrupted by COVID-19 stay-at-home orders (Pittsburgh: March 23 – May 8; Wake Forest: March 27 – May 8). No participants were newly recruited and enrolled during the COVID-19 lockdown period in the current sample.

7.3.4.2 Lifestyle and Health

Marital status (married/unmarried) was recorded at baseline. Participants also reported whether they had difficulties with driving (yes/no) or if they did not drive. As an indicator of socioeconomic well-being, participants further reported the degree to which their current financial needs were met (“very well,” “fairly well,” “poorly”). The Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire was used to assess self-reported frequency and duration of engagement in various physical activities (e.g., walking, sports, gardening, housework).\(^5\)\(^2\) We used caloric expenditure per week in all activities as a measure of self-reported energy expenditure from physical activity.

Self-rated health was assessed using a 5-point Likert scale (“excellent”, “very good”, “fair”, “poor”). Participants further reported whether they were ever diagnosed with the following conditions and the responses were summed to produce a total count: diabetes, stroke, myocardial
infarction, heart failure, lung disease (e.g., Chronic Obstructive Pulmonary Disease, chronic bronchitis, asthma), non-skin cancer, peripheral vascular disease, chronic kidney disease or renal failure, osteoporosis, and arthritis. Participants were asked to bring all prescription medications they had taken in the past 30 days to the Day 1 visit and the total number was recorded.

Depressive symptoms were measured using the 10-item Centers for Epidemiologic Studies Depression Scale (CES-D), with higher scores indicating greater depressive symptoms (possible range: 0-30). A cutoff score of ≥10 was used to indicate significant depressive symptoms. Global cognition was measured using the Montreal Cognitive Assessment (MoCA), with a score <26 indicating potential cognitive impairment. Height and weight were measured to calculate body mass index (BMI, kg/m²).

7.4 Statistical Approach

Descriptive statistics were assessed using means and standard deviations for continuous variables, as well as frequencies and percentages for categorical variables. Differences between life space constriction groups (i.e., unable to leave town without assistance) were assessed using Wilcoxon rank-sum tests for continuous variables and chi-square tests for categorical variables. Scatterplots with loess curves were used to assess linearity of associations between fitness/fatigability measures and life-space mobility.

To evaluate our study aims, we used multiple linear regressions with life space mobility score as the outcome. Because this study was cross-sectional, it is more plausible that demographic characteristics (e.g., age, sex, early life education) are true confounders, given the temporal precedence of these variables. In contrast, more proximate lifestyle and health factors may be either
confounders or mediators, as they likely have complex, reciprocal relationships with fitness/fatigability and life-space mobility. Adjusting for potential mediators may result in a more conservative estimate of association. Models were therefore sequentially adjusted for covariate groups. Model 1 was age-adjusted (years). Model 2 (demographic) further included gender (man/woman), education (≤high school, some college/college degree, some graduate/graduate degree), race (white/nonwhite), and whether the visit occurred on or after March 16, 2020 (i.e., COVID-19 lockdown indicator). Model 3 (lifestyle/health) further included marital status (married/unmarried), whether financial needs were met (“very well,” “fairly well/poorly,” missing/refused), driving difficulty (no difficulty vs. has difficulty or doesn’t drive), self-reported physical activity (CHAMPS kcal/week), self-rated health (excellent/very good vs. good/fair/poor), number of medical conditions (0, 1, ≥2), number of medications (0-2, 3-4, ≥5), depressive symptom categories (CES-D<10, CES-D≥10, missing/refused), potential cognitive impairment (MoCA<26), and BMI.

For our first aim, we tested models where each continuous exposure measure (VO$_2$peak, RPE, PFS Physical, PFS Mental) and the categorical fatigability indicators (RPE≥10, PFS Physical≥15, PFS Mental≥13, composite of all three) were included separately in the above models. For our second aim, we further tested for moderation of the fitness and life-space relationship by fatigability severity. We included interaction terms for VO$_2$ Peak and fatigability category, and we reported stratified estimates of the associations between VO$_2$ Peak and life-space for each fatigability group (e.g., RPE≥10 and <10). Model assumptions were evaluated using plots of predictors versus fitted life space scores (linearity), Q-Q plots (normally distributed residuals), and plots of residuals versus fitted scores (constant error variance).
8.0 RESULTS

8.1 Differences in Participant Characteristics by Life-Space Constriction

Most participants reported high life-space mobility on average (M=82.5±18.7, range: 30-120) and only 27% (n=105) of the sample had constricted life-space (i.e., unable to leave their town without assistance; Table 1). Compared to participants without life-space constriction (n=282), those with life-space constriction reported higher average depressive symptoms (4.6 vs. 3.9), higher average number of medical conditions (1.5 vs. 1.2) and poorer self-rated health. These participants were also less likely to report having their financial needs met “very well”. Participants with life-space constriction had significantly lower self-reported physical activity (2.6 vs. 4.1 kcal/week). They also had significantly lower physical functioning, measured by the SPPB (9.1 vs. 10.1) and gait speed on the usual-paced 400-meter walk (1.00 vs. 1.04 m/s). While life-space constriction was not more common among those whose study visits occurred during the COVID lockdown period (45% vs. 44%), average life-space composite scores were significantly lower among those who participated during the COVID lockdown period (84.5±18.8 vs. 80.0±18.3, Wilcoxon rank-sum z = 2.38, p=.017).

VO₂peak was negatively associated with fatigability measures, including RPE (ρ=-.41), PFS Physical (ρ=-.35), and PFS Mental (ρ=-.22, p<.001 for all; Table 2). RPE was positively correlated with PFS Physical (ρ=.29) and PFS Mental (ρ=.25), and the PFS Physical and Mental subscales were highly correlated with each other (ρ=.61, p<.001 for all).
Table 1: Participant Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th></th>
<th></th>
<th>Life-Space Mobility</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (SD)</td>
<td>Min</td>
<td>Max</td>
<td>M (SD)</td>
<td>M (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-space Composite Score</td>
<td>82.5 (18.7)</td>
<td>30</td>
<td>120</td>
<td>19.7 (4.1)</td>
<td>18.8 (4.4)</td>
<td>0.024</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO_{2peak}</td>
<td>19.5 (4.2)</td>
<td>12</td>
<td>35.9</td>
<td>18.5 (1.9)</td>
<td>18.7 (2.1)</td>
<td>0.459</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steady-state RPE</td>
<td>8.5 (2.0)</td>
<td>6</td>
<td>18</td>
<td>8.5 (1.9)</td>
<td>8.7 (2.1)</td>
<td>0.56</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFS Physical score</td>
<td>16.8 (8.3)</td>
<td>0</td>
<td>40</td>
<td>16.4 (8.2)</td>
<td>18.0 (8.7)</td>
<td>0.533</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PFS Mental score</td>
<td>8.0 (7.9)</td>
<td>0</td>
<td>38</td>
<td>8.0 (7.7)</td>
<td>7.9 (8.4)</td>
<td>1.181</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>76.4 (5.0)</td>
<td>70</td>
<td>94</td>
<td>76.2 (4.9)</td>
<td>77.0 (5.2)</td>
<td>0.138</td>
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<td></td>
</tr>
<tr>
<td>Depressive Symptoms (CES-D)</td>
<td>4.1 (3.4)</td>
<td>0</td>
<td>17</td>
<td>3.9 (3.3)</td>
<td>4.6 (3.4)</td>
<td>0.040</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Number of Medical Conditions</td>
<td>1.3 (0.9)</td>
<td>0</td>
<td>4</td>
<td>1.2 (0.9)</td>
<td>1.5 (0.9)</td>
<td>0.007</td>
<td></td>
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<tr>
<td>Number of Medications</td>
<td>4.4 (3.4)</td>
<td>0</td>
<td>20</td>
<td>4.2 (3.2)</td>
<td>4.8 (4.0)</td>
<td>0.286</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MoCA</td>
<td>24.8 (2.9)</td>
<td>13</td>
<td>30</td>
<td>25.0 (2.8)</td>
<td>24.3 (3.3)</td>
<td>0.181</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>28.0 (4.6)</td>
<td>18.7</td>
<td>39.5</td>
<td>28.1 (4.5)</td>
<td>27.6 (4.8)</td>
<td>0.334</td>
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<tr>
<td>SPPB (score)</td>
<td>10.0 (1.6)</td>
<td>4</td>
<td>12</td>
<td>10.1 (1.6)</td>
<td>9.7 (1.7)</td>
<td>0.018</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400M Walk Time (usual pace, m/s)</td>
<td>1.03 (0.16)</td>
<td>0.5</td>
<td>1.5</td>
<td>1.04 (0.15)</td>
<td>1.00 (0.17)</td>
<td>0.010</td>
<td></td>
<td></td>
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<tr>
<td>Physical Activity (CHAMPS, kcal/week)</td>
<td>3.70 (3.25)</td>
<td>0</td>
<td>32.2</td>
<td>4.10 (3.50)</td>
<td>2.60 (2.06)</td>
<td>&lt;.001</td>
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<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
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<th></th>
<th>Not Constricted to</th>
<th>Constricted to</th>
<th></th>
<th></th>
<th></th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td></td>
<td></td>
<td>Town</td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Site: Wake Forest (vs.</td>
<td>215 (56)</td>
<td>166 (59)</td>
<td>49 (47)</td>
<td>Pittsburgh</td>
<td>0.032</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Women (vs. men)</td>
<td>220 (57)</td>
<td>153 (54)</td>
<td>67 (64)</td>
<td></td>
<td>0.092</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nonwhite Race</td>
<td>44 (11)</td>
<td>29 (10)</td>
<td>15 (14)</td>
<td></td>
<td>0.270</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Visited during COVID lockdown (vs.</td>
<td>170 (44)</td>
<td>123 (44)</td>
<td>47 (45)</td>
<td>not)</td>
<td>0.840</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.238</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High school</td>
<td>59 (15)</td>
<td>39 (14)</td>
<td>20 (19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some college/college degree</td>
<td>203 (52)</td>
<td>146 (52)</td>
<td>57 (54)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Some graduate/graduate degree</td>
<td>125 (32)</td>
<td>91 (34)</td>
<td>28 (27)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married (vs. non-married)</td>
<td>199 (51)</td>
<td>154 (55)</td>
<td>45 (43)</td>
<td></td>
<td>0.040</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No driving difficulty (vs. has</td>
<td>373 (96)</td>
<td>276 (98)</td>
<td>97 (92)</td>
<td>difficulty)</td>
<td>0.010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good/fair self-rated health (vs.</td>
<td>140 (36)</td>
<td>92 (33)</td>
<td>48 (46)</td>
<td>excellent/very good</td>
<td>0.017</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Financial Needs Met (very well vs.</td>
<td>240 (62)</td>
<td>186 (66)</td>
<td>54 (51)</td>
<td>fairly well/poorly)</td>
<td>0.018</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tbody>
</table>

Note. Life-space constriction operationalized as being able to leave town without assistance. Life-space scores could range from 0 to 120. RPE = Borg Rating of Perceived Exertion (range: 6-20), PFS = Pittsburgh.
Fatigability Scale (range: 0-50), CES-D = Centers for Epidemiologic Studies Depression Scale (range: 0-30), MoCA = Montreal Cognitive Assessment (range: 0-30), BMI = body mass index, SPPB = Short Performance Physical Battery (range: 0-12), CHAMPS = Community Healthy Activities Model Program for Seniors inventory

Table 2: Bivariate Spearman Correlations between Fitness and Fatigability Measures

<table>
<thead>
<tr>
<th></th>
<th>VO2peak</th>
<th>Steady-state RPE</th>
<th>PFS Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2peak</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steady-state RPE</td>
<td>-0.41</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>PFS Physical</td>
<td>-0.35</td>
<td>0.29</td>
<td>--</td>
</tr>
<tr>
<td>PFS Mental</td>
<td>-0.22</td>
<td>0.25</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Note. All significant at p<.001. RPE = Borg Rating of Perceived Exertion, PFS = Pittsburgh Fatigability Scale.

8.2 Independent Fitness and Fatigability Measures and Life-Space Mobility

Exploratory scatterplots suggested that the association between fitness and life-space mobility was nonlinear. The association appeared significantly greater at the lower end of the distribution of VO2peak scores and then plateaued towards the upper end of the distribution (Figure 4A). We therefore modeled this association as a linear spline with a knot at 18, based on visual inspection of where the slope began to plateau. A VO2peak of 18 mL/min/kg has been established as a functional cut-point for high vs. low VO2peak in older adults. There was no evidence of nonlinearity for the associations between the fatigability measures and life-space mobility (data not shown).
Figure 4: Linear Spline Models of Fitness on Life-Space Mobility for the Overall Sample (A) and Stratified by Fatigability Group (B)

Note. Points represent observed VO\textsubscript{2}peak and life-space scores. Solid lines represent associations between observed VO\textsubscript{2}peak and fitted life-space scores from unadjusted linear spline models. The spline knot was placed at a VO\textsubscript{2}peak of 18 mL/kg/min. Dotted line represents exploratory loess smoother of association between VO\textsubscript{2}peak and life-space scores.
8.2.1 Cardiorespiratory Fitness

For the lower end of the fitness range (VO$_2$peak ≤ 18), each 1-mL/kg/min greater VO$_2$peak was associated with a 3.0-point greater life-space score in the age-adjusted model (95% CI: 1.61, 4.42, p<.001; Table 2). A 3-point change in Life Space Assessment score is roughly equivalent to leaving the house an additional 1-3 days per week, depending on functional assistance. This association was attenuated but remained significant after adjusting for demographic (B=2.73, 95% CI: 1.30, 4.17, p<.001) and lifestyle/health confounders (B=2.17, 95% CI: 0.68, 3.67, p=.005). For the upper end of the VO$_2$peak range (VO$_2$peak ≥ 18), VO$_2$peak had a negative association with life-space mobility only in the fully adjusted model (B=-0.74, 95% CI: -1.45, -0.02, p=.043), but the estimate became non-significant after removing one outlier with very low life-space (30 points, z-score = -2.8) and very high fitness (30.8 mL/kg/min, z-score = 2.7) (p>.05).

8.2.2 Perceived Fatigability

Each 1-point greater PFS Physical score was associated with a 0.33-point lower life-space score in the age-adjusted model (95% CI: -0.55, -0.11, p=.004; Table 2). This association remained significant after adjusting for demographic confounders (B=-0.39, 95% CI: -0.61, -0.16, p=.001), but was no longer significant after full adjustment (p>.05; Table 2, Model 3). Each 1-point greater PFS Mental score was associated with a 0.28-point lower life-space score in the age-adjusted model (95% CI: -0.52, -0.04, p=.020) in the age-adjusted model. This association was attenuated but remained significant after adjusting for demographic confounders (B=-0.26, 95% CI: -0.50, -0.02, p=.001), but was no longer significant after full adjustment (p>.05). Steady-state RPE was not associated with life-space mobility (p>.05; Table 2).
Table 3: Associations between Continuous Fitness/Fatigability Measures and Life-Space Composite Score

<table>
<thead>
<tr>
<th></th>
<th>Model 1 (Age-adjusted)</th>
<th>Model 2 (+Demographics)</th>
<th>Model 3 (+Lifestyle/Health)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>95% CI</td>
<td>P-value</td>
</tr>
<tr>
<td>Fitness (splines) *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2peak≤18</td>
<td>3.02</td>
<td>(1.61, 4.42)</td>
<td>&lt;.001***</td>
</tr>
<tr>
<td>VO2peak&gt;18</td>
<td>-0.30</td>
<td>(-0.92, 0.33)</td>
<td>0.352</td>
</tr>
<tr>
<td>Perceived Fatigability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steady-state RPE</td>
<td>-0.63</td>
<td>(-1.59, 0.33)</td>
<td>0.200</td>
</tr>
<tr>
<td>PFS Physical</td>
<td>-0.33</td>
<td>(-0.55, -0.11)</td>
<td>0.004**</td>
</tr>
<tr>
<td>PFS Mental</td>
<td>-0.28</td>
<td>(-0.52, -0.04)</td>
<td>0.029*</td>
</tr>
</tbody>
</table>

Note. N=387. p<.05*, p<.01**, p<.001***; Beta estimates represent difference in Life Space Assessment score per 1-unit greater score on the fitness or fatigability measure. Fitness and fatigability measures were each entered separately for each model.

*a Model with spline terms for VO2peak fit significantly better than model with single term (likelihood-ratio test: χ²=13.6, p<.001).

b estimate becomes non-significant after removing one outlier with very low life-space score (30 points, z-score = -2.8) and very high fitness (30.8 mL/kg/min, z-score = 2.7).

Model 1 was age-adjusted.

Model 2 was adjusted for demographics: gender, study site, race/ethnicity, education, and COVID-19 visit status

Model 3 was further adjusted for lifestyle/health factors: marital status (married vs. unmarried), financial needs (met “poorly/fairly well”, “very well”, or missing/refused), driving status (has difficulty vs. no difficulty), self-reported physical activity (CHAMPS kcal/wk), self-reported health (“good/fair” vs. “excellent/very good”), depressive symptoms (CESD-10<10, CES-D>=10, missing/refused), BMI, potential cognitive impairment (MoCA<26), number of medical conditions (0, 1, 2+) and prescription medications (0-2, 3-4, 5+).

RPE = Ratings of Perceived Exertion; PFS = Pittsburgh Fatigability Scale
8.3 Fatigability Composite and Life-Space Mobility

Using the established cut-points for each fatigability measure, we found that 35% of participants met no fatigability threshold (n=134; Figure 3). Most participants (n=230, 59%) met the threshold for PFS Physical (≥15), but substantially fewer met the thresholds for RPE fatigability (≥10; n=94, 24%) and/or PFS Mental (≥13; n=92, 24%). Ten percent of participants (n=37) met the criteria for all three fatigability measures.

Participants meeting all three fatigability criteria had a 7.02-point lower life-space score (95% CI: -13.37, -0.68, p=.030; Table 3). A 7-point difference in Life Space Assessment score is roughly equivalent to leaving the house an additional 4-6 days per week, depending on functional assistance. This difference in life-space score was about 2-3 points greater than the difference for the individual fatigability thresholds alone (B=-3.4 to -4.9, Table 3). The association remained significant after adjusting for demographics (B=-7.59, 95% CI: -13.84, -1.34, p=.017), but was attenuated and no longer significant after further adjusting for lifestyle and health variables (B=-3.37, 95% CI: -9.94, 3.19, p=.313).
Table 4: Associations between Fatigability Severity Cut-Points and Life-Space Composite Score

<table>
<thead>
<tr>
<th>Individual Cut-points</th>
<th>Model 1 (Age-adjusted)</th>
<th>Model 2 (+Demographics)</th>
<th>Model 3 (+Lifestyle/Health)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>B</td>
<td>95% CI</td>
</tr>
<tr>
<td>Steady-state: RPE≥10</td>
<td>94 (24)</td>
<td>-3.43</td>
<td>(-7.81, 0.94)</td>
</tr>
<tr>
<td>PFS Physically15</td>
<td>230 (59)</td>
<td>-4.41</td>
<td>(-8.24, -0.59)</td>
</tr>
<tr>
<td>PFS Mentally13</td>
<td>92 (24)</td>
<td>-4.88</td>
<td>(-9.26, -0.50)</td>
</tr>
<tr>
<td>Composite Cut-point</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPE≥10 &amp; PFS Physically15 &amp; PFS Mentally13</td>
<td>37 (10)</td>
<td>-7.02</td>
<td>(-13.37, 0.38)</td>
</tr>
</tbody>
</table>

Note. N=387; p<.05*. Beta estimates represent difference in Life Space Assessment score comparing those with higher vs. lower fatigability. Fatigability measures were each entered separately for each model.

Model 1 was age-adjusted.

Model 2 was adjusted for demographics: gender, study site, race/ethnicity, education, and COVID-19 visit status

Model 3 was further adjusted for lifestyle/health factors: marital status (married vs. unmarried), financial needs (met “poorly/fairly well”, “very well”, or missing/refused), driving status (has difficulty vs. no difficulty), self-reported physical activity (CHAMPS kcal/wk), self-reported health (“good/fair” vs. “excellent/very good”), depressive symptoms (CESD-10<10, CES-D>=10, missing/refused), BMI, potential cognitive impairment (MoCA<26), number of medical conditions (0, 1, 2+) and prescription medications (0-2, 3-4, 5+).

RPE = Ratings of Perceived Exertion; PFS = Pittsburgh Fatigability Scale
8.4 Moderation of the Fitness-Life-Space Relationship by Fatigability

In models including interactions between fitness and fatigability strata, associations between fitness and life-space mobility were stronger for those with more severe physical fatigability as measured by steady-state treadmill RPE (Table 4, Figure 4B). For individuals with RPE≥10 and within the lower fitness range (VO₂peak <18), each 1-mL/min/kg greater VO₂peak was associated with a 3.3-point greater life-space score (95% CI: 1.06, 5.53, p-interaction=.078). There was no significant association between VO₂peak and life-space mobility for individuals with RPE<10 or in the upper range of fitness (VO₂peak≥18; p>.05). There was also no significant moderation of the association between fitness and life-space by PFS Physical or PFS Mental (p-interactions>.10, data not shown).
Table 5: Stratified Associations between Fitness and Life-Space Mobility by Fatigability Severity (Steady-state Treadmill Rating of Perceived Exertion)

<table>
<thead>
<tr>
<th>Fitness (VO2 Peak) ≤18</th>
<th>Stratified Model (Full adjustment)</th>
<th>95% CI</th>
<th>P-value (interaction)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher RPE (≥10)</td>
<td>3.30**</td>
<td>(1.06, 5.53)**</td>
<td>0.078</td>
</tr>
<tr>
<td>Lower RPE (&lt;10)</td>
<td>0.84</td>
<td>(-1.43, 3.10)</td>
<td></td>
</tr>
<tr>
<td>Fitness (VO2 Peak) &gt;18</td>
<td>0.386</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher RPE (≥10)</td>
<td>-0.39</td>
<td>(-2.40, 1.61)</td>
<td></td>
</tr>
<tr>
<td>Lower RPE (&lt;10)</td>
<td>-0.56</td>
<td>(-2.51, 1.40)</td>
<td></td>
</tr>
</tbody>
</table>

Note. N=387; p<.01**. Beta estimates represent difference in Life Space Assessment score per 1-mL/kg/min greater VO2peak. P-values are for interaction terms from models where each fitness spline by RPE interaction term was entered separately.

Model was adjusted for age, gender, study site, race/ethnicity, education, and COVID-19 visit status, lifestyle/health factors: marital status (married vs. unmarried), financial needs (met “poorly/fairly well”, “very well”, or missing/refused), and driving status (has difficulty vs. no difficulty), self-reported health (“good/fair” vs. “excellent/very good”), depressive symptoms (CESD-10<10, CES-D≥10, missing/refused), BMI, potential cognitive impairment (MoCA<26), number of medical conditions (0, 1, 2+) and prescription medications (0-2, 3-4, 5+).

RPE = Ratings of Perceived Exertion; PFS = Pittsburgh Fatigability Scale
9.0 DISCUSSION

We examined novel associations between a comprehensive set of fitness and fatigability measures and life-space mobility in community-dwelling older adults. First, we showed that lower fitness, measured by gold-standard VO\textsubscript{2peak}, was associated with lower life-space mobility. The association was stronger for those within the lower range of fitness scores (VO\textsubscript{2peak}≤18) than those with higher fitness scores (VO\textsubscript{2peak}>18). We further found that a composite measure of fatigability had larger associations with life-space mobility compared to individual fatigability measures alone (RPE, PFS Physical, PFS Mental), but associations for all fatigability measures were attenuated in fully adjusted models. Finally, we found a potential fitness-fatigability interaction, where those with both low fitness and high fatigability had the lowest life-space mobility. These findings build upon existing conceptual models of life-space mobility\textsuperscript{10} by suggesting that fitness and fatigability may be important, joint contributors to life-space in later life.

Fitness (i.e., aerobic capacity) contributes to efficiency of energy utilization and total energy available to engage in physical activity, which can vary in demand.\textsuperscript{38} The observed nonlinear association between fitness and life-space mobility may be due in part to the level of physical demand required for everyday mobility. VO\textsubscript{2peak} was measured during maximal exercise testing,\textsuperscript{16,25} and it is unlikely that individuals with moderate or high fitness would need to operate close to their maximum capacity when traveling in their everyday environments. This is in part due to the numerous, cross-cutting factors that influence life-space mobility and that could compensate for modest deficits in fitness,\textsuperscript{10} including psychosocial (e.g., social supports),\textsuperscript{4} environmental (e.g., access to transportation),\textsuperscript{3} and financial (e.g., income) factors.\textsuperscript{14} Yet, when
fitness falls below a critical threshold (defined here as VO$_{2\text{peak}}$ $\leq$ 18), it may become a more substantial barrier to mobility. The current findings support this interpretation, as we show that the association between fitness and life-space mobility for those within the lower range of fitness was significant, even after adjusting for potential compensatory factors (e.g., psychosocial, environmental, financial confounders).

Further, fatigability may impact life-space mobility by limiting one’s ability to respond to environmental challenges, potentially due to physical or mental exhaustion from completing daily tasks.$^{29,42}$ Prior work from the Osteoporotic Fractures in Men Study (MrOS) found that more severe fatigability (PFS Physical or PFS Mental) was significantly related to lower life-space mobility in community-dwelling older men.$^{42}$ Here we showed that more severe fatigability was associated with lower life-space mobility in a sample that included women and a wider age range of older adults. We further found that a composite measure of fatigability, incorporating fatigue ratings on both a single treadmill task (RPE) and range of imagined activities (PFS Physical and Mental), had stronger associations with life-space mobility than the individual measures alone. We observed that those who met established cut-points for each fatigability measure (RPE $\geq$ 10, PFS Physical $\geq$ 15, PFS Mental $\geq$ 13)$^{30}$ had 7-point lower life-space scores (versus 3.4-4.8 points lower for the individual measures). This difference was clinically meaningful$^{57}$ and remained significant when adjusting for demographic factors. These findings suggest that incorporating information from multiple fatigability assessments likely identified those with the most severe fatigability and ultimately at the highest risk of life-space constriction than if individual fatigability measures were used alone.

However, the associations between each fatigability measure and life-space mobility were attenuated and no longer significant in models that further accounted for lifestyle and health
factors. Although we intended to adjust for a comprehensive set of factors known to influence life-space mobility,\textsuperscript{10} some of the included lifestyle and health covariates may instead be mediators of the fatigability-life-space relationship. For example, depression has been associated with lower life-space mobility,\textsuperscript{3} but worsening fatigue may also be a precursor to more severe depression.\textsuperscript{58} Declines in physical activity may precede increases in fatigability,\textsuperscript{41,55} but greater fatigability may lead to further declines in activity by limiting physical functioning.\textsuperscript{31,34} Adjusting for such mediators may have attenuated the associations and resulted in more conservative estimates of the relationship between fitness/fatigability and life-space mobility. Longitudinal studies with repeated measurements are needed to tease apart whether these factors are confounders or mediators of the fatigability-life-space relationship. We plan to examine this in the future when longitudinal data are available in SOMMA.

We further investigated whether fitness and fatigability interacted in their associations with life-space mobility. We found potential evidence for this, where the relationship between fitness and life-space mobility was strongest for those also reporting higher fatigability (steady-state RPE≥10). There are multiple interpretations of this finding. First, fitness and fatigue are thought to influence one-another in a bi-directional cycle.\textsuperscript{38} Lower fitness may lead to poorer energy utilization or less total energy available to engage in physical activity, resulting in increased fatigue from activity of a set duration and intensity. Individuals likely adapt to this fatigue by reducing their activity levels (i.e., self-pacing), which in turn further reduces their fitness (e.g., from lack of exercise) and begins the cycle again. Thus, having both lower fitness on a maximal exercise task and higher fatigability on a steady-state task may signal that an individual is farther along in this vicious cycle and at higher risk of life-space constriction.
Second, perceived fatigability may also capture mental processes (e.g., perceived task demands, perceived capacity)\textsuperscript{29} that could moderate the degree to which low fitness impacts fatigue and activity. For example, perceived capacity (i.e., self-efficacy) includes one’s beliefs in their capabilities to satisfy task demands and has been shown to influence behaviors like physical activity.\textsuperscript{43} Individuals with lower fitness (i.e., low objective capacity), who also feel that they are unable to meet the demands of their environment given their lower fitness (i.e., low perceived capacity), may be especially vulnerable to life-space constriction. The current findings support this interpretation, as we found the association between fitness and life-space mobility was significant primarily for those with higher fatigability and within the lower range of VO\textsubscript{2}peak.

This study was limited by its cross-sectional design, as we were unable to rule out reverse causation (e.g., lower life-space contributing to lower fitness or higher fatigability) or establish temporality of the associations between fitness/fatigability, life-space mobility, and included covariates. We also excluded participants with missing CPET or covariate data, leading to potential selection bias, although this likely produced more conservative estimates of association. Participants were also primarily White and highly educated. The current results should be replicated in more diverse samples (e.g., racially, socioeconomically).

This study also had several strengths. We used a gold-standard measure of fitness (i.e., VO\textsubscript{2}peak) that was collected in a large, epidemiologic cohort of older adults. We also had access to multiple validated measures of perceived fatigability, allowing us to create a composite measure of fatigability that had a more robust association with life-space mobility. We considered multiple potential demographic, lifestyle, and health confounders thought to contribute to life-space mobility.\textsuperscript{10} Finally, our sample included women and had a wider age range than participants in MrOS, enabling us to replicate our prior findings in broader demographic groups.
Life-space mobility is a holistic indicator of well-being in later life. We found that lower fitness was related to lower life-space mobility, independent of demographic, lifestyle, and health characteristics. This relationship was nonlinear and strongest within the lower range of fitness scores. While fatigability was not independently associated with life-space mobility after full adjustment, it moderated the fitness-life-space relationship. Individuals with both lower fitness and higher fatigability reported the lowest life-space mobility, suggesting that these individuals are the most vulnerable to life-space constriction. Ultimately, public health interventions that target this high-risk group may mitigate further functional declines resulting from life-space constriction.
References


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