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ORIGINAL ARTICLE

Construct validation of the vitality capacity domains 'energy and metabolism' and 'neuromuscular function' in relation to locomotor capacity and quality of life in community-dwelling middle-aged and older adults

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Abstract Vitality capacity (VC) reflects a physiological state and is a determinant domain of intrinsic capacity but has so far remained mainly theoretical. This study validates the vitality capacity domains 'energy and metabolism' and 'neuromuscular function' and examines its link to locomotor capacity and quality of life (QoL). Exploratory factor analysis (EFA) was performed on the combined dataset from the Fatigue Resistance AMErsfoort study (FRAME, n = 1000) and the Fatigue Plot study (FATPLOT,n = 620). Confirmatory factor analyses (CFA) were subsequently performed on data from the AMersfoort COhort study on functional decline, Healthy aging and Frailty (AMCOHF,n = 367) and the BrUssels sTudy on The Early pRedictors of FraiLtY (BUTTERFLY,n = 491), to validate VC in both middle-aged and older adults. Linear hierarchical regression analysis was used to investigate the relationship between VC, locomotor capacity, and QoL. EFA indicated a one-factor model and CFA validated this with good model fit in the dataset (BUTTERFLY) (Robust CFI; 0.960, SRMR: 0.040) and (AMCOHF) (Robust CFI; 0.942, SRMR: 0.055). This model validated

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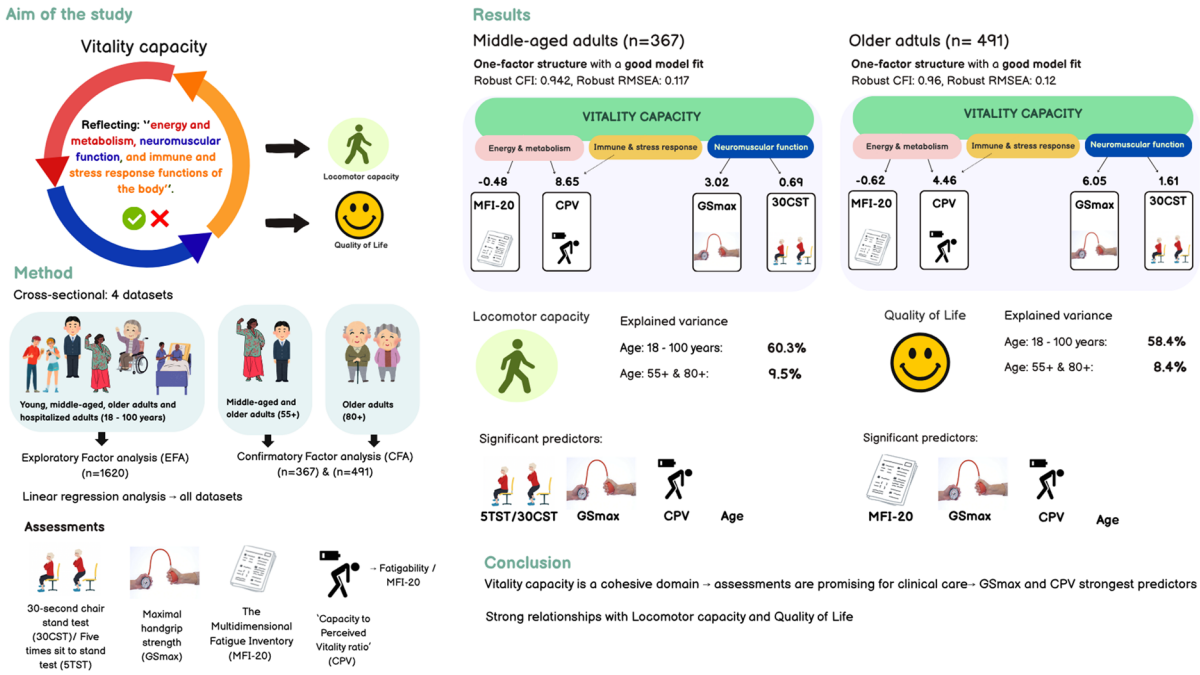
maximal grip strength (GSmax), 30-s chair stand test (30CST), Multidimensional Fatigue Inventory (MFI-20) and Capacity to Perceived Vitality ratio physical (CPV-physical) to measure VC. Several assessments show a significant relationship with locomotor capacity and QoL. This study indicated that VC is a coherent domain and has a relationship with locomotor capacity and QoL.

Graphical Abstract



Keywords Vitality capacity · Neuromuscular function · Fatigability · Intrinsic capacity · Healthy ageing

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Introduction

Healthy Ageing extends beyond the absence of disease, emphasizing maintaining an individual's potential to preserve functional abilities as they age [1]. Intrinsic capacity (IC)—defined as *"the composite of all the physical and mental capacities that an individual can draw on at any point in time"*—is at the heart of this concept, encompassing locomotor, sensory, cognitive, psychological, and vitality capacity (VC) [2]. Sufficient IC in each domain is essential to cope with environmental challenges (physical, mental, …) for maintaining functional ability, defined as *"all the health-related attributes that enable people to be and to do what they have reason to value"*, irrespective of the presence of disabilities or health conditions. VC is proposed as a determinant domain representing the underlying physiological component – and thus directly influencing the

other domains—of IC [3]. A consensual working definition [4] defines VC as "*a physiological state (due to normal or accelerated biological ageing processes) resulting from the interaction between multiple physiological systems, reflected in (the level of) energy and metabolism, neuromuscular function, and immune and stress response functions of the body*". However, at present, VC remains mainly a theoretical construct in need of further empirical validation.

The interacting physiological systems of VC are closely linked to healthy ageing. In the domain of energy and metabolism, fatigue reflects reduced physiological reserve and contributes to a heightened risk of functional decline and negative health outcomes [5]. Neuromuscular function, often assessed through grip strength with a hand-held dynamometer [6], has shown associations with negative health outcomes such as disability (odds ratio [OR]1.78 [95%CI 1.28–2.48]) and mortality (OR1.79 [1.26–2.55]) [7]. (Low-grade) inflammation serves as a biomarker of the immune and stress response functions of the body, and increased levels of High-sensitivity C-reactive protein (hs-CRP) have been associated with reduced physical quality of life (QoL) [8]. To maintain functional ability, these physiological systems play a crucial role. For instance, muscle strength and fatigue levels affect the ability to climb stairs or walking, demonstrating how VC can influence locomotor capacity and QoL, both important for healthy ageing. Early detection of VC deterioration may enable timely prevention to preserve or enhance IC, thereby supporting healthy ageing.

This study aimed to validate the theoretical construct of VC, by examining whether empirical data were consistent with the proposed theoretical model. In addition, the study investigated the relationships between VC and key indicators of healthy ageing, specifically locomotor capacity and QoL, which are essential for maintaining health and functionality during ageing. Given the cross-sectional design, the analyses focused on assessing construct validity and associations, rather than causal inferences.

Methods

Study design and participants

Baseline data were obtained from the AMersfoort COhort study on functional decline, Healthy aging and Frailty (AMCOHF), the BrUssels sTudy on The Early pRedictors of FraiLtY (BUTTERFLY), the Fatigue Plot study (FATPLOT), and the Fatigue Resistance AMErsfoort study (FRAME).

AMCOHF is an ongoing prospective cohort in the Netherlands including independently living individuals aged 55–75 years who understand Dutch [9]. BUTTERFLY, a longitudinal cohort in Belgium, included community-dwelling individuals aged 80 years and older who were able to understand Dutch or French. In AMCOHF & BUTTERFLY, participants were required to be non-frail (i.e., robust or pre-frail) at inclusion. FRAME and FATPLOT are cross-sectional involving participants aged 18–100 years. Comprehensive participant characteristics are outlined in Supplementary Table S1.

The medical ethical committee of the University Hospital of the Vrije Universiteit Brussel approved BUTTERFLY (UZ Brussel, B.U.N.143201421976) and FATPLOT (UZ Brussel, B.U.N.143201523331). The medical ethical committee Zuyderland-Zuyd approved FRAME (METC-Z 14-N-154 & 14-T-161) and AMCOHF (METC-Z: NL70141.096.19). All participants provided written informed consent.

Vitality Capacity

Based on the operationalization of VC, the selected assessments reflect its underlying physiological systems: 'energy and metabolism' and 'neuromuscular function' [4].

Neuromuscular function

Knee extensor strength was assessed by the 30-s chair stand test (30CST), or the five times sit-to-stand test (5TST), depending on cohort-specific availability. For the 30CST the participants started seated on a chair and were encouraged to complete as many full stands as possible within 30 s [15]. For the 5TST, participants started seated with arms across the chest and were instructed to stand up and sit down five times as quickly as possible. Timing started from the initial seated position and ended at the final standing position after the fifth stand [16]. Maximal hand grip strength (GSmax) was assessed using the Martin Vigorimeter (KLS Martin Group, Tuttlingen, Germany). The Martin Vigorimeter reliably assesses handgrip strength (ICC 0.70) in middle-aged and older adults,

and has been proposed as an appropriate measure of the neuromuscular component of vitality capacity [6]. Participants squeezed the large bulb with their dominant hand as hard as possible, and the highest score of three attempts was registered [11].

Energy & metabolism

The Multidimensional Fatigue Inventory (MFI-20) was used to measure fatigue with twenty questions encompassing five domains: mental fatigue, reduced motivation, reduced activity, physical fatigue, and general fatigue [10]. Each item was scored on a 5-point Likert scale, a higher score (20–100) indicating higher fatigue. Muscle fatigability was assessed by the fatigue resistance (FR) test measured as the time at which grip strength drops to 50% of the GSmax during a sustained maximal contraction [12]. In the FATPLOT study, among 620 participants (young: n = 204, middle-aged: n = 222, older: n = 168, hospitalized: n = 50) (Supplementary Table S1), the FR test was conducted using a modified pneumatic handgrip system (original rubber bulb of the Martin Vigorimeter connected to a Unik 5000 pressure gauge [GE, Germany]) [11].

Grip Work (GW) represents the physiologic work delivered by the handgrip muscles during the FR test [13]. It is calculated as $GW = FR$ x 0.75 x $GSmax$, representing the area under the strength-time curve, and further divided by body weight (GWBW) to normalize for differences in body size [13].

A 'Capacity to Perceived Vitality ratio' (CPV) was calculated by dividing GWBW by the MFI-20 total score [14]. The Capacity to Perceived Vitality ratio physical (CPV-physical), was calculated as GWBW divided by the physical fatigue subdomain score of the MFI-20. Within the concept of VC, we assumed that CPV can serve as a measurement, with higher values indicating better VC.

Locomotor capacity

Honvo et al. conducted a systematic review to identify valid and reliable assessments of locomotor capacity, defined as *"a state of the musculoskeletal system that encompasses endurance, balance, muscle strength, muscle function, muscle power, and joint function"* [17]. Timed-Up-and-Go test (TUG) was selected to assess locomotor capacity. Participants started seated, and time was recorded for standing up, walking three meters to a wall, returning, and sitting down [18].

Quality of life

The 3-level EQ-5D version (EQ-5D-3L) was used for measuring QoL and consists of five questions covering five health dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [19]. Each dimension has three levels: none, moderate and extreme problems. The overall is scored between −0.312 (extreme problems) and 0.947 (no problems), which represents the preferences of the Dutch population [20]. The EQ-5D-3L also includes an EQ-VAS where participants rated their own health on a scale from 0 (worst imaginable health) to 100 (best imaginable health) [19].

The Medical Outcome Study Short-form (MOS-SF-20) was used where participants rated their own health and QoL over the previous four weeks [21], including 20 questions, divided into six domains: Physical functioning, Role functioning, Social functioning, Mental Health, Health Perceptions, and Physical Pain. These were transformed into a standardized 100-point scale, with a higher score representing better health, while for physical pain the scoring was inversed [22].

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics for Mac, Version 29.0 (IBM Corp., Armonk, NY, USA). Participant characteristics are reported as mean ± standard deviation (SD). Sex differences were examined with independent *t*-tests and proportions with chi-square tests. Correlations and age- and sex-adjusted partial correlations were calculated in FRAME/FATPLOT, AMCOHF, and BUTTERFLY to assess associations among VC measures (GSmax, GW, GWBW, 5TST/30CST, MFI-20, CPV, and CPV-physical). An exploratory factor analysis (EFA; Oblimin rotation, Kaiser normalization) identified underlying structure. In cases of multicollinearity ($r > 0.80$), one variable was excluded. The Kaiser–Meyer–Olkin value had to exceed 0.50, and factor retention was based on eigenvalues > 1.0 and scree plot inspection. To evaluate robustness, confirmatory factor analysis (CFA) was conducted in R (R Core Team, 2021) using the BUTTERFLY and

AMCOHF datasets to confirm the structure identified in FRAME/FATPLOT. Parameters were estimated using robust maximum likelihood, and standardized latent variable coefficients were reported. Model fit was evaluated using the Comparative Fit Index (CFI), Root Mean Square Error of Approximation (RMSEA, 90% CI), and Standardized Root Mean Square Residual (SRMR). Good fit was defined as CFI > 0.90, RMSEA < 0.08, and SRMR < 0.08; excellent fit as CFI ≥ 0.95 [23]. The chi-square statistic was reported but not used as a fit index due to its sensitivity to large samples. Hierarchical linear regression assessed the predictive value of VC (GSmax, CPV-physical, MFI-20, 30CST/5TST) on locomotor capacity and QoL, adjusting for age and sex. For AMCOHF and BUTTERFLY, robust model outcomes and standardized latent variables were interpreted. Statistical significance was set at $p < 0.05$. Standardized β and R^2 values of 0.10/0.02, 0.30/0.13, and 0.50/0.26 were interpreted as small, moderate, and large effects [24].

Missing data were assessed for all variables, and analyses included participants with complete data. In BUTTERFLY, HGmax was available for 491 of 494 participants. For AMCOHF (n = 367) and FRAME/FATPLOT (n = 1620), no missing data were present. The EFA sample (n = 1620) exceeded recommended thresholds for stable factor extraction. CFA was performed on two independent samples (n = 491 and n = 367), both meeting accepted criteria for model estimation. A priori power analysis using G*Power indicated that, for multiple linear regression with eight predictors, assuming a medium effect size ($f^2 = 0.15$) and power = 0.95, at least 160 participants per cohort were required.

Results

AMCOHF participants were the youngest and the BUTTERFLY participants the oldest. Additionally, significant cohort-by-sex interactions were observed for all variables except the Mini-Mental State Exam (MMSE). The participants' characteristics and cohort differences are shown in Table 1.

For the EFA in FRAME/FATPLOT (n = 1620), GSmax, GW_{BW}, MFI-20, 5TST, CPV and CPV-physical were considered as possible variables, and several models were assessed (Supplementary material Figure S1, S2, and S3). Correlations and partial correlations (corrected for age and sex) can be found in the supplementary material Table S2, S3 and S4. The best model included GSmax, MFI-20, 5TST and CPV-physical, indicating a single-factor solution with an eigenvalue of 2.36, explaining 59% of the variance. This revealed the path coefficients for GSmax (0.76), MFI-20 (−0.80), 5TST (−0.73), and CPV-physical (0.78), as shown in Fig. 1.

The CFA drawing on the BUTTERFLY data (n = 491) included GSmax, MFI-20, 30CST and CPV-physical. This confirmed a one-factor structure with good model fit based on CFI and SRMR ($X^2(2)$: 15.25, $p < 0.001$, Robust CFI; 0.96, Robust RMSEA [90%]:0.12[0.07–0.17], SRMR:0.04). RMSEA fit values were above the cutoff. The following path coefficients were found, including the 30CST (1.61), GSmax (6.05), MFI-20 (−0.62) and CPV-physical (4.46) (Fig. 2A). The CFA drawing on the AMCOHF data (n = 367) also confirmed a one-factor structure with a good model fit based on CFI and SRMR ($^X2(2)$:11 98, $p = 0.003$, Robust CFI:0.942, Robust RMSEA [90%]:0.117[0.060–0.184], SRMR:0.055). RMSEA fit values were above the cutoff. The following path coefficients were found, including the 30CST (0.69), GSmax (3.02), MFI-20 (−0.48) and CPV-physical (8.65) (Fig. 2B).

A hierarchical linear regression analysis was performed to investigate the relationship between VC and locomotor capacity, measured with the TUG. In FRAME/FATPLOT, GSmax, 5TST, MFI-20, CPV-physical, age, and sex were considered as predictors. The best model explained 60.3% of the variance in TUG times (R^2 adjusted = 0.603, $p < 0.001$) (Table 2), indicating the 5TST (β = 0.619), GSmax (β = −0.092), CPV-physical (β = −0.041), and age (β = 0.147) as significant predictors. Data from AMCOHF and BUTTERFLY were combined to perform a hierarchical linear regression analysis, considering the 30CST, GSmax, CPV-physical, MFI-20, age, and sex as predictors (Table 2). The best model explained 9.5% of the variance in TUG times (R^2 adjusted = 0.095, $p < 0.001$), indicating that the 30CST (β = −0.301) and age (β = −0.092) were significant predictors (Table 2).

To assess the relationship between VC and QoL, a hierarchical linear regression analysis was conducted using the MOS-SF-20 health perceptions scale as the measure of QoL. In FRAME/FATPLOT the 5TST, GSmax, CPV-physical, MFI-20, TUG,

Table 1 Participants characteristics

	FRAME/FATPLOT									BUTTERFLY			AMCOHF		
Variables	Men	Women	Total	Subacute rehabilitating older adults aged ≥ 70 years	Acute hospitalized older adults aged ≥ 70 years	Older adults aged ≥ 70 years living or receiving day-care in a nursing home	Community-dwelling subjects with high probability of physical frailty aged > 50 years	Community-dwelling subjects aged > 3 0years	Young, healthy subjects aged 18–30 years (reference group)	Men	Women	Total	Men	Women	Total
Number (%)	814 (50.1)	806 (49.9)	1620 (100)	100(100)	100(100)	182(100)	238(100)	488(100)	512(100)	259 (52.4)	235 (47.6)	494 (100)	190 (51.9)	177 (48.1)	367 (100)
Age (years)	54.4 ± 24.4	54.4 ± 24.5	54.4 ± 24.5$^	80.6 ± 6.7	80.7 ± 6.4	81.5 ± 7.5	70.3 ± 11.6	56.5 ± 16.9	25.1 ± 3.0	83.4 ± 3.1*	82.9 ± 2.7	83.1 ± 2.9$^	66.3 ± 5.8*	64.7 ± 5.3	65.5 ± 5.6$^
Weight (kg)	83.4 ± 4.1*	71.9 ± 14.5	77.7 ± 15.4	75.1 ± 15.4	75.9 ± 15.6	75.7 ± 13.9	83.5 ± 17.9	79.5 ± 14.5	74.9 ± 14.4	78.3 ± 11.2*	65.2 ± 9.9	72.1 ± 12.5	84.0 ± 11.8*	69.8 ± 12.7	77.2 ± 14.1
Height (cm)	179.7 ± 7.8*	166.4 ± 7.6	173.1 ± 10.2^	169.4 ± 9.2	170.7 ± 10.2	169 ± 9.6	170.0 ± 10.4	173.7 ± 10.1	176.5 ± 9.2	170.3 ± 6.5*	157.8 ± 5.9	164.3 ± 8.8$	180.0 ± 7.2*	167.5 ± 6.1	174.0 ± 9.1
GSmax (kPa)	87.9 ± 32.7*	62.8 ± 24.4	75.5.7 ± 31.5$^	49.0 ± 17.0	40.0 ± 19.0	45.1 ± 16.4	60.4 ± 20.7	82.2 ± 26.5	98.8 ± 25.3	67.5 ± 15.2	46.7 ± 10.7	57.6 ± 16.8$^	95.6 ± 19.4*	68.6 ± 12.7	82.2 ± 21.5
GripWork (kPa×s)	3076.0 ± 2248.7*	2309.8 ± 1887.2	2695.3 ± 2107.0$^	1465.2 ± 1046.0	921.9 ± 1009.6	1058.5 ± 963.4	1906.6 ± 1290.1	3841.9 ± 2172.2	3141.0 ± 2111.2	3406.2 ± 1834.9*	2532.5 ± 1650.0	2991.5 ± 1801.6$^	4810.4 ± 2255.4*	3805.4 ± 1954.2	4330.0 ± 2169.8$^
GripWork / body-weight (kPa× s/kg)	37.8 ± 28.2*	33.1 ± 27.3	35.5 ± 27.8$^	19.8 ± 12.9	12.3 ± 13.9	14.3 ± 12.9	23.5 ± 16.3	49.6 ± 29.2	42.3 ± 27.8	44.6 ± 25.3*	40.0 ± 26.5	42.4 ± 25.9$^	58.8 ± 30.0*	56.5 ± 30.7	57.7 ± 30.3
TUG test (s)	10.3 ± 7.4	11.1 ± 10.6	10.7 ± 9.1^	24.1 ± 16.2		22.3 ± 13.9	12.6 ± 6.0	7.3 ± 2.0	6.6 ± 1.0	7.01 ± 2.0*	8.2 ± 4.8	7.6 ± 3.8$	7.6 ± 1.5	7.3 ± 1.3	7.5 ± 1.4$
MFI (20–100)	45.3 ± 18.6	445.9 ± 18.1	45.6 ± 18.3^	59.1 ± 18.1	64.9 ± 17.7	57.3 ± 18.2	61.0 ± 13.4	37.0 ± 13.8	36.1 ± 11.3	44.8 ± 11.2	445.0 ± 14.3	33.3 ± 23.6$	47.6 ± 22.4	50.0 ± 22.0	48.7 ± 22.2
Capacity to Perceived Vitality ratio	1.0 ± 1.1	0.9 ± 1.0	1.0 ± 1.0^	0.4 ± 0.4	0.2 ± 0.4	0.3 ± 0.4	0.4 ± 0.3	1.6 ± 1.2	1.3 ± 1.0	9.0 ± 6.3*	6.6 ± 5.8	7.9 ± 6.2$	1.6 ± 1.3	1.4 ± 1.0	1.5 ± 1.1^
Capacity to Perceived Vitality ratio / physical domain MFI	5.5 ± 6.0*	4.7 ± 5.6	5.7 ± 6.1^	1.9 ± 1.8	1.2 ± 1.9	1.6 ± 2.0	1.8 ± 1.6	8.8 ± 6.8	7.6 ± 6.0	6.7 ± 05.4*	5.6 ± 5.1	6.2 ± 5.3$	9.2 ± 7.6	8.2 ± 6.9	8.7 ± 7.3^
5TST (s)	15.4 ± 9.7	15.1 ± 9.1	12.6 ± 8.3	21.5 ± 9.6	21.8 ± 12.3	23.9 ± 14.3	17.6 ± 7.2	10.1 ± 3.6	8.4 ± 2.1						
30CST (*n*)										13.1 ± 3.6*	12..0 ± 3.4	12. 6 ± 3.6	16.1 ± 4.2	15.6 ± 3.6	15.9 ± 4.0
MMSE (0–30)	27.0 ± 3.7	26.9 ± 4.1	27.0 ± 3.9	26.5 ± 3.6	25.2 ± 4.1	22.2 ± 5.4	28.3 ± 1.8	28.5 ± 1.8	29.4 ± 1.0				27.5 ± 0.1	27.7 ± 0.7	27.5 ± 2.0
MOCA										24.6 ± 2.8	24.3 ± 4.2	17.1 ± 11.6			
MOS-SF-20 health perceptions (0–100)	64.1 ± 27.9	64.0 ± 27.0	68.7 ± 26.6	45.6 ± 26.1	38.6 ± 25.3	59.5 ± 25.6	43.3 ± 24.0	79.9 ± 17.6	83.8 ± 14.9						
3-level EQ-5D (–0.312 - 0.947)													0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1
EQ-VAS (0–100)													84.5 ± 9.5	84.9 ± 8.8	84.7 ± 9.1

age and sex were considered as predictors. The best model had an explained variance of 58.4% (R^2 adjusted = 0.584, $p < 0.001$) (Table 3), indicating the MFI-20 (β = −0.677) and age (β = −0.086) as significant predictors. In AMCOHF, we investigated the relationship between VC and QoL, measured by the EQ-5D-3L, by considering the 30CST, GSmax, CPV-physical, MFI-20, TUG, age and sex as predictors (Table 3). The best model had an explained variance of 4.6% (R^2 adjusted = 0.046, $p < 0.001$), indicating GSmax (β = 0.243) as a significant predictor. In a subsequent model, QoL was assessed using the EQ-VAS as the dependent variable and considering the same predictors (Table 3). The best model explained 8.4% of the variance (R^2 adjusted = 0.084, $p < 0.001$) and indicated a significant relationship with CPV-physical (β = 0.296) and age (β = 0.139).

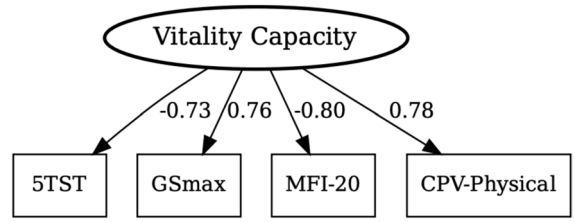
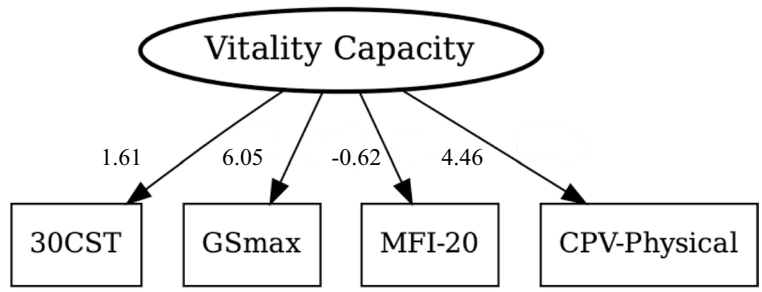


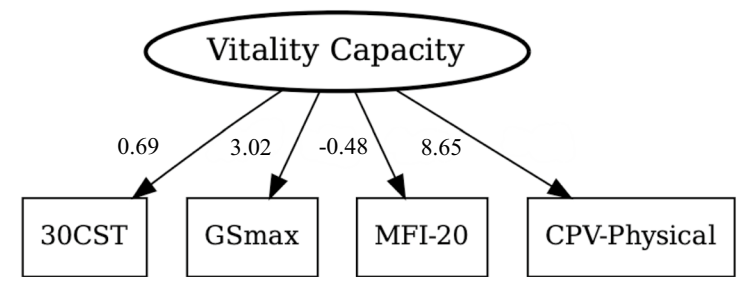
Fig. 1 Exploratory factor analysis in the FRAME/FATPLOT study. Vitality capacity was modelled as a latent variable with four observed indicators: 5TST (Five Times Sit-to-Stand Test), GSmax (maximum hand grip strength), MFI-20 (Multidimensional Fatigue Inventory), and CPV-physical (Capacity to Perceived Vitality ratio physical)

Discussion

This study examined the validity of VC and its relationship with locomotor capacity and QoL. Both EFA and CFA supported a one-factor solution with good model fit based on CFI and SRMR, indicating that VC forms a cohesive domain when including the 30CST, GSmax, CPV-physical, and MFI-20. Although RMSEA values did not meet conventional cut-offs, this index often overestimates misfit in models with few degrees of freedom, such as the present four-indicator model (two degrees of freedom), and greater emphasis on CFI and SRMR is therefore recommended [25]. This issue is particularly relevant in clinical research, where efficient test batteries often result in models with few indicators. Additionally, the lower bounds of the RMSEA confidence intervals were within acceptable ranges. Therefore, additional sensitivity analyses were not performed, as they were unlikely to improve model evaluation and would



A BUTTERFLY study



B AMCOHF study

Fig. 2 Confirmatory factor analysis in the AMCOHF & BUTTERFLY studies. Path coefficients standardized with respect to the latent variable vitality capacity are presented for four observed indicators: 30CST (30-s chair stand test), GSmax (maximum handgrip strength), MFI-20 (Multidimensional Fatigue Inventory), and CPV-physical (Capacity to Perceived Vitality ratio physical)

Table 2 Hierarchical linear regression analysis on locomotor capacity

	B	B 95CI	SE B	β	t	p	Adjusted R^2	Std. error of the estimate	R square change
FRAME and FATPLOT model 1	**2.747**	**1.066–4.428**	**.857**		**3.206**	**0.001**	**0.605**	**3.672**	
5TST (sec)	.447	0.416–0.478	0.016	.605	28.077	< 0.001			
GSmax (kPa)	−0.018	−0.030—−0.007	0.006	−0.094	−3.093	0.002			
MFI-20 (20–100)	0.021	0.006–0.036	0.008	0.060	2.725	0.007			
CPV-physical	−0.013	−0.054 – 0.027	0.020	−0.014	−0.658	0.511			
Sex	−0.182	0.021–0.047	0.252	−0.016	−0.722	0.471			
Age (years)	0.034	0.021–0.047	0.006	0.137	5.239	< 0.001			
FRAME and FATPLOT model 2	**3.537**	**1.951—5.123**	**0.808**		**4.376**	**< 0.001**	**0.603**	**3.681**	**−0.002**
5TST (sec)	0.457	0.427–0.488	0.015	0.619	29.501	< 0.001			
GSmax (kPa)	−0.018	−0.029—−0.006	0.006	−0.092	−3.041	0.002			
CPV-physical	−0.038	−0.074- −0.002	0.018	−0.041	−2.071	0.039			
Sex	−0.189	−0.684 – 0.305	0.252	−0.016	−0.751	0.453			
Age (years)	0.036	0.024–0.049	0.006	0.147	5.642	< 0.001			
AMCOHF and BUTTERFLY model 1	**11.745**	**9.396–14.093**	**1.197**		**9.815**	**< 0.001**	**0.104**	**2.781**	
30CST (n)	−2.15	−0.269—−0.161	0.027	−0.298	−7.822	< 0.001			
GSmax(kPa)	−0.004	−0.011 – 0.003	0.004	−0.047	−1.226	0.220			
MFI-20 (20–100)	0.019	0.007–0.031	0.006	0.120	3.041	0.002			
CPV-physical	0.009	−0.033 – 0.050	0.021	0.018	0.404	0.686			
Sex	−0.352	−0.733 – 0.030	0.194	−0.060	−1.811	0.071			
Age (years)	−0.022	–0.044–0.001	0.011	−0.072	−1.912	0.056			
AMCOHF and BUTTERFLY model 2	**13.199**	**11.036–15.362**	**1.102**		**11.976**	**< 0.001**	**0.095**	**2.795**	**−0.009**
30CST (n)	−0.216	−0.271—−0.162	0.028	−0.301	−7.844	< 0.001			
GSmax(kPa)	−0.002	−0.009 – 0.005	0.003	−0.024	−0.626	0.531			
CPV-physical	−0.027	−0.062 – 0.008	0.018	−0.058	−1.510	0.131			
Sex	−0.351	−0.734 – 0.032	0.195	−0.060	−1.798	0.073			
Age (years)	−0.028	−0.05—−0.006	0.011	−0.092	−2.465	0.014			

Dependent variable: Timed Up and Go test (seconds). *FRAME* Fatigue Resistance AMErsfoort study, *FATPLOT* Fatigue Plot study, *AMCOHF* AMersfoort COhort study on Functional Decline, Healthy Ageing and Frailty, *BUTTERFLY* BrUssels sTudy on The Early pRedictors of Frailty. *B* unstandardised regression coefficient, *95% CI* 95% confidence interval for B, *SE B* standard error of B, *β* standardised regression coefficient, *t* t-value of predictor, *p p*-value of the t-test; adjusted R^2 = variance in the dependent variable explained by the predictors, adjusted for their number; standard error of the estimate = standard deviation of residuals. *5TST* five times sit-to-stand test, *GSmax* maximum handgrip strength, *MFI-20* Multidimensional Fatigue Inventory, *CPV-physical* Capacity to Perceived Vitality ratio physical, *30CST* 30-s chair stand test

either lack theoretical justification or further reduce degrees of freedom. The results suggest that physiological systems are interlinked, with changes in neuromuscular function closely associated with changes in energy and metabolism. These findings align empirical data with the theoretical model of VC, particularly the neuromuscular function and energy and metabolism domains, with GSmax and CPV-physical showing the strongest associations. Notably, factor loadings exceed 1.0. This is expected because coefficients were standardized with respect to the latent variable, vitality capacity, and are therefore not constrained to fall between − 1 and 1, particularly when indicators are measured on different scales.

VC has been described in the literature as an underlying domain, influencing the other domains

Table 3 Hierarchical linear regression analysis on quality of life

	B	B 95% CI	SE B	β	t	p	Adjusted R^2	Std. error of the estimate	R^2 change
FRAME and FATPLOT Model 1 MOS-SF-20 Health perceptions	77.688	68.912–86.465	4.474		17.364	<.001	.584	16.123	
5TST (sec)	−0.052	−0.181 – 0.077	0.066	−0.017	−0.789	0.430			
GSmax (kPa)	0.038	−0.012 – 0.087	0.025	0.046	1.490	0.136			
MFI-20 (20–100)	−0.986	−1.050—−0.921	0.033	−0.677	−30.121	<.001			
CPV-physical	0.120	−0.055 – 0.295	0.089	0.030	1.342	0.180			
Sex	1.344	−0.780 – 3.468	1.083	0.027	1.241	0.215			
Age (years)	−0.090	−0.145—−0.035	0.028	−0.086	−3.200	0.001			
AMCOHF Model 1 EQ-5D-3L	0.645	0.472–0.818	0.088		7.328	<.001	0.046	0.0973	
30CST (n)	0.645	−0.001 – 0.004	0.001	0.056	1.007	0.315			
GSmax (kPa)	0.001	0.000–0.002	0.000	0.243	3.237	0.001			
MFI-20 (20–100)	0.000	−0.001 – 0.001	0.000	0.003	0.053	0.958			
CPV-physical	0.002	0.000–0.003	0.001	0.116	1.783	0.075			
Sex	−0.023	−0.052- 0.005	0.014	−0.117	−1.610	0.108			
Age (years)	0.002	0.000–0.004	0.001	0.106	1.779	0.076			
AMCOHF Model 1 EQ-5D-3L-VAS	65.329	49.753- 80.904	7.920		8.249	<.001	0.084	8.760	
30CST (n)	0.011	−0.234- 0.257	0.125	0.005	0.091	0.928			
GSmax (kPa)	0.014	−0.049 – 0.076	0.032	0.032	0.438	0.662			
MFI-20 (20–100)	0.015	−0.034 – 0.064	0.025	0.037	0.599	0.549			
CPV-physical	0.376	0.217–0.535	0.081	0.296	4.658	<.001			
Sex	−1.551	−4.113 – 1.010	1.302	−0.085	−1.191	0.234			
Age (years)	0.227	0.039–0.415	0.096	0.139	2.377	0.018			
AMCOHF Model 2 EQ-5D-3L-VAS	65.841	49.060–82.622	8.533		7.716	<.001	0.081	8.772	−0.003
30CST (n)	.005	-.253–0.263	.131	.002	0.37	.970			
GSmax (kPa)	.014	-.049-.076	.032	.032	.435	.664			
MFI-20 (20–100)	.015	-.034-.065	.025	.037	.600	.549			
CPV-physical	.376	.217-.536	.081	.296	4.647	<.001			
Sex	−1.531	−4.108–1.045	1.310	-.084	−1.169	.243			
Age (years)	.227	.039-.415	.096	.139	2.374	.018			
TUG (sec)	−0.56	-.727-.616	.341	-.009	-.163	.871			

Dependent variables: EQ-5D-3L and EQ-5D-3L-VAS. *FRAME* Fatigue Resistance AMErsfoort study, *FATPLOT* Fatigue Plot study, *AMCOHF* AMersfoort COhort study on Functional Decline, Healthy Ageing and Frailty. *B* unstandardised regression coefficient, *95% CI* 95% confidence interval for B, *SE B* standard error of B, *β* standardised regression coefficient, *t* t-value of predictor, *p* p-value of the t-test, adjusted R^2 = variance in the dependent variable explained by the predictors, adjusted for their number; standard error of the estimate = standard deviation of residuals; R^2 change = change in explained variance compared with the previous model. *30CST* 30-s chair stand test, *GSmax* maximum handgrip strength, *MFI-20* Multidimensional Fatigue Inventory, *CPV-physical* Capacity to Perceived Vitality ratio physical, *MOS-SF* Medical Outcomes Study Short Form, *TUG* Timed Up and Go test

of IC [3]. Its relationship with locomotor capacity showed higher explained variance in FRAME/FATPLOT compared to BUTTERFLY and AMCOHF, likely due to the broader age range in FRAME/FATPLOT (18–100 years). As the TUG is a relatively simple mobility test, variability is typically limited in younger and middle-aged adults, whereas greater variability is expected with increasing age due to declines in muscle strength, balance, and mobility. This likely explains the observed difference in

explained variance, as greater variability across the broader age range enhances model discrimination. Similar explained variances were observed for CPV and CPV-physical, but CPV-physical is more clinically efficient as it uses only the four-item physical fatigue subdomain of the MFI-20 instead of the full 20-item scale. VC related with locomotor capacity, with the 5TST and 30CST showing the strongest associations. The 5TST was a strong and the 30CST a moderate predictor of locomotor capacity, with both primarily reflecting knee extensor strength. VC showed a strong association with QoL, with the MFI-20 demonstrating a large effect, indicating greater fatigue is linked to lower QoL. CPV-physical showed a moderate association, suggesting it is a meaningful QoL predictor. As the decade of healthy ageing aims to maintain an individual's functional abilities [1] these are relevant biomarkers of VC, especially since smart ehealth systems such as Eforto® [26] allow easy (self)assessment of GSmax and CPV.

While the theoretical model of VC is relatively novel and supported by limited existing research, the outcomes of this study align with earlier work. Lu et al. (2023) reported that participants with higher handgrip strength ($\beta = -0.011$;95% CI[−0.023, 0.000]) or lower inflammation ($\beta = -0.015$; 95% CI[−0.028, −0.002]) showed fewer IADL difficulties at follow-up [27]. Moreover, VC predicted locomotor capacity over time, underscoring its role as a key domain of IC [27]. Similarly, Koivunen et al. (2023) validated the IC framework using grip strength as the indicator of VC, and the overall IC composite score was significantly associated with functional decline and mortality [5]. Specifically, they found that a one-point decrease in IC-score was associated with a 10% higher probability of functional decline over six years (OR = 0.90; 95% CI[0.89–0.92]). A higher IC score was also linked to lower mortality risk (HR = 0.94;95% CI[0.93–0.95]) [5]. In addition, prior research has shown that muscle endurance and fatigue, which are used as instruments for VC in this study, are good predictors of activities of daily living and gait speed after a one year follow up in older adults [28]. Collectively, these findings are promising and support further exploration of the potential predictive ability of VC for healthy ageing.

A key strength of this study is the validation of VC across diverse cohorts. This enhances the model's suitability for early detection of VC decline in clinical practice, as intrinsic capacity declines before functional problems occur [3].This increases the potential for preventive interventions to preserve IC. Another strength of this study is the inclusion of simple and affordable tests, feasible in low-income countries [29], promoting health equity. Nevertheless, this study has limitations. Using the 5TST and 30CST to assess VC may have influenced the latent variable structure, as these tests reflect not only muscle strength but also balance and endurance. Future studies could use handheld dynamometry to assess neuromuscular function more directly, as it isolates muscle strength and may better represent VC. The absence of measures for immune and stress response systems also warrants further exploration. Including CPV-physical may partly capture these aspects, given its association with inflammatory biomarkers such as hsCRP and IL-6 [30]. Given the cross-sectional design, the predictive value of VC should be further examined in longitudinal research.

Conclusion

This study supports vitality capacity, operationalized by the neuromuscular function and energy and metabolism domains, as a cohesive domain represented by GSmax, 30CST/5TST, MFI-20, and CPV-physical, which showed strong associations with locomotor capacity and QoL. These findings support integrating VC into healthcare strategies that promote healthy ageing and guide interventions to improve and maintain vitality across the lifespan.

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Author contributions IB and VK conceptualized this study and supervised the data curation, the data analysis and the writing of the manuscript, and reviewed and edited the final draft. IB, VK, JD, LDD, AD, SC, DH, and AVDW contributed to the data collection. FL did the formal data analysis and wrote the original draft. IB, VK, JD, LDD, DB, AD, SL, EG, BB, SC, DH, AVDW, GR, BJ and APG revised the manuscript. IB and VK accessed and verified the data.

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Data availability The datasets and/or data analyses used during the current study are available from the corresponding author upon reasonable request.

Declarations

None declared.

Data sharing Data sharing is not applicable to this article.

Competing interest The authors have no competing interests to declare.

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