Methodological approaches to estimate physical resilience in older adults: a comparison across two clinical settings

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RESEARCH PAPER

Methodological approaches to estimate physical resilience in older adults: a comparison across two clinical settings

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Abstract

Introduction: Various methodological approaches exist to estimate physical resilience in older adults (phenotype, expected recovery, adapted ageing), but their comparative performance remains unclear. This study evaluated their agreement and predictive performance across two clinical contexts.
Methods: We applied three methodological approaches in two cohorts: older adults receiving chemotherapy (TENT) and those presenting with acute illness at the emergency department (APOP). Physical functioning was assessed using Katz Activities of Daily Living and Lawton Instrumental Activities of Daily Living scales. The phenotype approach measured functional change after the health stressor; the expected recovery approach compared actual to predicted recovery based on clinical characteristics; and the adapted ageing approach assessed baseline function relative to expected levels given clinical risk profile. Outcomes at 12 months included mortality and a composite endpoint of functional decline, quality of life decline or mortality. Agreement was assessed using Cohen's kappa and predictive performance using area under the curve (AUC).
Results: The TENT cohort included 330 patients (median age 75 years; 43% female) and APOP included 2111 patients (median age 78 years; 54% female). Agreement between approaches was poor to moderate ($\kappa = -0.10$ to 0.64). All approaches showed only moderate discriminative ability for 12-month mortality (AUC 0.55–0.69) and composite outcomes (AUC 0.52–0.66). The physical resilience approaches provided limited added discrimination beyond simple predictors: functional score at follow-up (AUC 0.65–0.69) and age (AUC 0.48–0.67).
Conclusion: Various physical resilience approaches identified different patient groups as resilient and demonstrated limited prognostic value. Current approaches may inadequately capture the dynamic construct of physical resilience; higher-frequency longitudinal measures may better quantify physical resilience for clinical practice.

Keywords: physical resilience; expected recovery; residual; geriatrics; older people

Key Points

- Physical resilience approaches classify older adults differently, showing poor-to-moderate agreement across cohorts.
- Prognostic performance of resilience approaches for 12-month outcomes is modest in both chemotherapy and emergency presentations.
- Simple clinical predictors (age, follow-up functional score) match or outperform resilience approaches for outcome discrimination.

Introduction

Physical resilience has emerged as an important concept in geriatric medicine, representing an individual's capacity to resist, or recover from, functional decline after a health stressor [1]. Therefore, the assessment of physical resilience may serve as a valuable tool in predicting the clinical trajectory of patients during the course of disease treatment. By understanding a patient's physical resilience profile, clinicians could better anticipate recovery patterns, adapt treatment strategies and potentially enhance physical resilience through targeted interventions [2, 3]. This is particularly relevant in older populations, where heterogeneity in biological age and functional reserve can lead to markedly different outcomes even among patients with similar age, baseline characteristics and disease severity [4].

Despite growing recognition of its clinical importance, there is no standardised method for quantifying physical resilience. Several methodological approaches have been proposed to operationalise and estimate physical resilience in clinical populations [5, 6]. These include the phenotype approach, which estimates physical resilience based on observable recovery patterns and functional characteristics following a stressor [2, 7, 8]; and residual-based approaches, which encompass two distinct methods. First, the expected recovery approach, which quantifies physical resilience as post-stressor recovery exceeding predicted recovery trajectories and second the 'adapted ageing' approach [6, 9], which defines physical resilience as better-than-expected baseline function (pre-stressor) given an individual's health status and risk profile. Although these are all approaches aimed at estimating physical resilience, their agreement and relative performance in predicting clinical outcomes remains unclear. Notably, no studies to date have systematically compared these different methodological approaches for predicting clinical outcomes in older patients across multiple clinical settings.

Therefore, this study aims to evaluate the agreement in classifying physical resilience between different methodological approaches, and to compare their ability to predict clinical outcomes across different clinical contexts.

Methods

We analysed three methodological approaches for estimating physical resilience in two distinct cohorts. Below, we first describe the two cohorts and the available measurements, followed by a description of each physical resilience approach and its specific implementation in both cohorts.

Description of cohorts

We analysed the different methodological approaches in two distinct cohorts representing different populations and health stressors: older cancer patients undergoing chemotherapy treatment (TENT cohort) and older adults presenting to emergency departments (EDs) with acute illness (APOP cohort).

Triage of elderly needing treatment cohort

To assess the physical resilience approaches in older patients with cancer undergoing chemotherapy, we used data from the Triage of Elderly Needing Treatment (TENT) study. This multicentre cohort included patients aged 70 years and older who were scheduled to undergo intensive treatment in seven medical centres across the Netherlands. The study was approved by the medical ethics committee of the Leiden University Medical Centre and registered in the Dutch Trial Register (NL8107). All participants provided written informed consent. Detailed study procedures have been described previously [4, 10, 11]. For this analysis, we only included patients who received chemotherapy for any malignant neoplasm between December 2015 and August 2024. We limited the selection to patients receiving chemotherapy to improve population and stressor homogeneity.

At baseline, patients underwent screening with the G8 frailty screening tool [12] and the Six-Item Cognitive Impairment Test [13], followed by a geriatric assessment (GA) evaluating functional status (Katz Activities of Daily Living (ADL) and Lawton Instrumental Activities of Daily Living (IADL) scales [14, 15]), quality of life (EQ-5D-3L and EQ-VAS [16]), nutritional status (Mini Nutritional Assessment [17]), mood (Patient Health Questionnaire-2 [18]) and comorbidities (Charlson Comorbidity Index [19]). Functional status and quality of life were reassessed at 6 and 12 months after treatment initiation. GA results were categorised into four domains: somatic, functional, psychological and social. A domain was classified as abnormal if one or more component tests were abnormal. The somatic domain included comorbidity (Charlson Comorbidity Index $\geq$1), polypharmacy ($\geq$5 medications) and malnutrition (mini nutritional assessment <12). The functional domain included falls within the past 6 months, institutionalisation and functional dependency (ADL score $\geq$ 2, or IADL

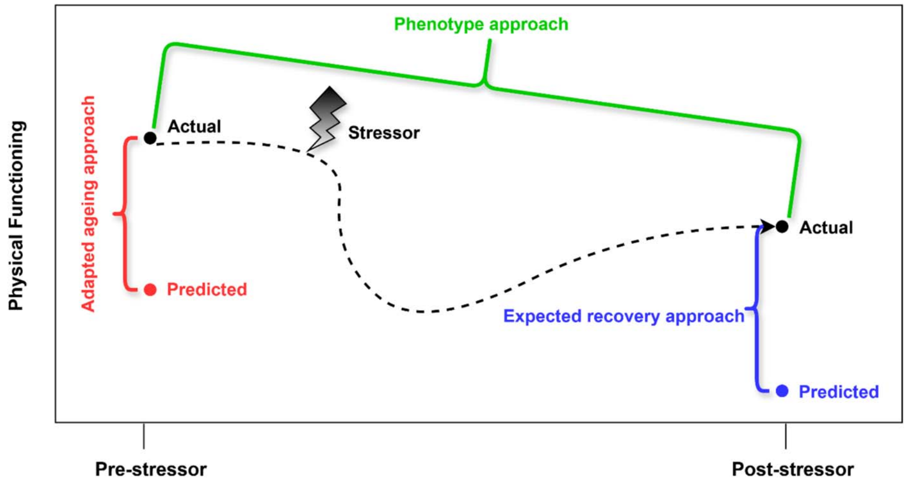

Figure 1. Conceptual diagram illustrating three approaches for estimating physical resilience: phenotype (green, functional change after stressor), expected recovery (blue, actual vs. predicted recovery) and adapted ageing (red, baseline function vs. expected levels). Lightning bolt indicates health stressor; dotted line shows a trajectory of physical functioning.

score ≤ 4 for men/≤ 7 for women). The psychological domain included dementia, history of delirium and cognitive impairment (Six-Item Cognitive Impairment Test >7). The social domain was classified as abnormal when patients lived alone.

Acute presenting older patient cohort

To assess the physical resilience approaches in older patients presenting to the ED, we used data from the Acute Presenting Older Patient (APOP) study, a prospective cohort of patients aged 70 years and older presenting to EDs at four Dutch hospitals between 2014 and 2017. Medical ethics committees waived formal approval as data collection followed routine care. Written informed consent was obtained from patients or relatives. Detailed procedures have been described previously [20, 21].

Baseline assessment included functional status (Katz ADL; assessed for the situation two weeks before ED visit), and polypharmacy (use of ≥ 5 medications, self-reported). Functional status was reassessed 90 days and 1 year after the ED visit using the Katz ADL index. Mortality data up to 1 year after the ED visit was obtained from municipal records.

Physical resilience approaches

We applied and compared three methodological approaches for estimating physical resilience (i) the phenotype approach, (ii) the expected recovery approach, and (iii) the adapted ageing approach. The approaches are described below, and a conceptual visual representation of these approaches is presented in Figure 1.

Phenotype approach

This approach estimates physical resilience by measuring the functional trajectory after a health stressor [2, 7, 8]. We operationalised the phenotype approach by calculating the change in physical functioning between pre- and post-stressor timepoints (physical functioning at follow-up minus baseline physical functioning). In the TENT cohort, we calculated the change in IADL score between baseline and 6 months. In the APOP cohort, we calculated the change in ADL score between baseline and 3 months.

Expected recovery approach

This approach estimates physical resilience by comparing predicted recovery based on clinical characteristics to actual recovery [5]. We operationalised the expected recovery approach by applying a three-step process. First, we created a linear regression model to predict physical functioning (ADL or IADL) at follow-up using baseline clinical variables. Second, we calculated the expected physical functioning for each individual participant using this model. Finally, we derived the expected recovery residual (physical functioning at follow-up minus predicted physical functioning at follow-up). For example, if based on a participant's baseline clinical characteristics the model predicts an IADL score of 3 at follow-up, but their actual IADL score at follow-up was 5, the residual would be +2, indicating better-than-expected recovery (higher physical resilience). Conversely, if their actual IADL score at follow-up was 1, the residual would be −2, indicating worse-than-expected recovery (lower physical resilience). In the TENT cohort, we predicted IADL at 6 months using age, sex, baseline IADL, additional treatments (yes/no), mono or polychemotherapy, treatment intent (curative versus palliative) and Charlson Comorbidity Index as covariates. In the APOP cohort, we predicted ADL at 3 months using age, sex, baseline ADL, polypharmacy, institutionalisation, living arrangement and dementia diagnosis as covariates.

Adapted ageing approach

This approach estimates physical resilience by assessing whether baseline physical functioning differs from expected levels of physical functioning based on clinical characteristics. We operationalised this approach by applying the same three-step process as the expected recovery approach, but used baseline physical functioning (ADL or IADL) as the regression outcome rather than follow-up function, finally deriving the adapted ageing residual (physical functioning at baseline minus predicted physical functioning at baseline). For example, if based on a participant's age and comorbidity profile the model predicts a baseline IADL score of 4, but their actual baseline IADL score was 6, the residual would be +2, indicating better-than-expected baseline function (higher physical resilience). Conversely, if their actual baseline IADL score was 2, the residual would be −2, indicating worse-than-expected baseline function (lower physical resilience), suggesting accelerated functional decline prior to the health stressor. In the TENT cohort, we predicted baseline IADL using age, sex, polypharmacy and Charlson Comorbidity Index as covariates. In the APOP cohort, we predicted baseline ADL using age, sex, polypharmacy, institutionalisation, living arrangement and dementia diagnosis as covariates.

Clinical predictors

As benchmarks for the physical resilience approaches, we used the simple clinical predictors age and physical functioning at follow-up (IADL at 6 months for TENT and ADL at 3 months for APOP). In the TENT cohort only, we also used a frailty classification based on the number of abnormal GA domains (range 0–4) as a benchmark.

Outcomes

All physical resilience approaches and clinical predictors were evaluated for their ability to predict outcomes at 12 months from study inclusion (Figure 2). We assessed two clinical outcomes at 12 months: mortality (yes/no) and a composite endpoint, which was defined as decline in quality of life and/or physical functioning, or mortality.

In the TENT cohort, quality of life decline was defined as a decrease of 0.06 or greater in EQ-5D-3L index score or 7 or more points on the EQ-VAS from baseline to 12 months [22]. Physical functioning decline was defined as a 1-point increase in ADL dependency, new institutionalisation or a 1-point decrease in IADL score [23]. In the APOP cohort, physical functioning decline was defined as a 1-point increase in Katz ADL dependency or new institutionalisation. Quality of life was not measured in the APOP cohort and was therefore excluded from the composite endpoint in this cohort.

Statistical analysis

Sociodemographic and clinical variables at baseline were summarised using descriptive statistics, including means and 95% confidence intervals for normally distributed continuous variables, medians with interquartile ranges (IQR) for skewed continuous variables, and frequencies with percentages for categorical variables as appropriate.

To assess whether the different approaches classify the same patients as having high, intermediate or low physical resilience, we divided cohorts into tertiles based on each physical resilience approach and computed pairwise Cohen's kappa coefficients for all combinations of approaches.

Predictive performance of the three physical resilience approaches and clinical comparator predictors were assessed using receiver operating characteristic (ROC) curve analysis. All physical resilience approaches were evaluated for their ability to predict outcomes measured at 12 months from study inclusion. Area under the ROC curve (AUC) values were calculated, ranging from 0.5 (no discrimination) to 1.0 (perfect discrimination).

Missing data were handled using complete case analysis. To improve comparability among the different approaches, only participants with complete baseline and follow-up data required for all three approaches were included in the analyses.

Descriptive analyses were performed using SPSS version 25 (IBM Corp Released 2017, IBM SPSS Statistics for Windows, Version 25). All other analyses were performed in R (version 4.3.1).

Results

Between December 2015 and August 2024, 2183 patients with cancer were eligible for the TENT cohort. Of these, 1535 (70%) provided informed consent and were enrolled. Following exclusion of patients who did not receive chemotherapy (n = 1085) or had missing data required for the physical resilience approaches (n = 120), 330 patients remained for analysis. For the APOP cohort, 3147 patients were eligible, with 2629 (84%) providing informed consent and enrolling in the study. After excluding patients with missing data needed for the physical resilience approaches (n = 518), 2111 patients were included in the analysis (Supplementary Figure 1).

Table 1 presents the baseline characteristics for both cohorts. The TENT cohort comprised participants with a median age of 75 years (IQR 72–78), of whom 43% were female. The most common tumour sites were upper gastrointestinal (31%), lower gastrointestinal (20%) and gynaecologic (15%); 50% had locally advanced disease (cT3-4) and 29% received palliative chemotherapy (Supplementary Table 1). The APOP cohort had a median age of 78 years (IQR 74–83), with 54% female participants. The most common presenting complaints were minor trauma (32%), malaise (17%) and chest pain (16%); 45% were admitted to hospital (Supplementary Table 2). Both cohorts demonstrated relatively preserved pre-stressor functional status, with median ADL scores of 0 (IQR 0–1; in APOP assessed for the situation 2 weeks before ED presentation).

Supplementary Table 3 presents the distribution of physical resilience measures and clinical predictors across both cohorts. The phenotype approach showed minimal functional change in both cohorts, with a mean difference of 1.42 (95% CI 1.01–1.82) in the TENT cohort and 0.16 (95%

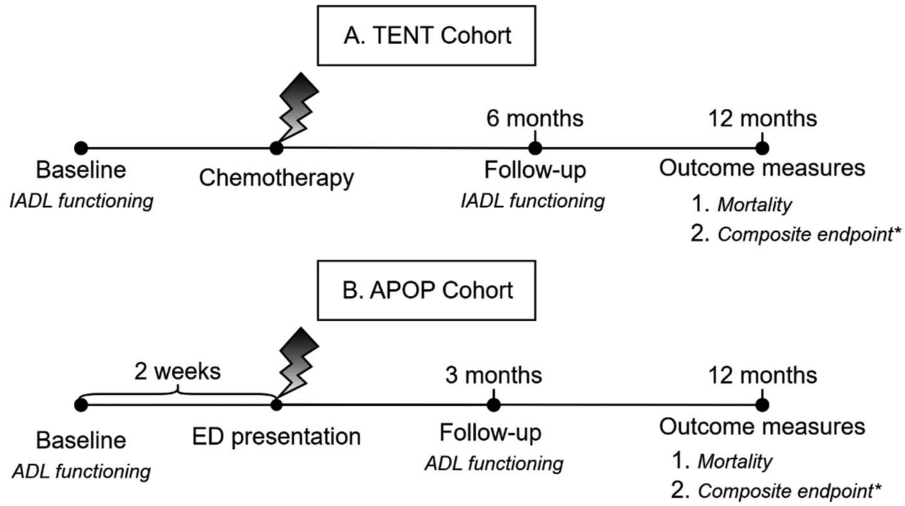

Figure 2. Timeline of data collection for (A) TENT cohort and (B) APOP cohort. Lightning bolt indicates health stressor. * TENT: Decrease in quality of life or decrease in physical functioning or mortality; APOP: Decrease in physical functioning or mortality. Abbreviations: IADL—Instrumental Activities of Daily Living; ADL—Activities of Daily Living; ED—Emergency department

Table 1. Baseline characteristics of included participants, stratified by cohort.

Characteristic	TENT (n = 330)	APOP (n = 2111)
Age, years, median (IQR)	75 (72–78)	78 (74–83)
Female sex, n (%)	142 (43%)	1135 (54%)
Institutionalised, n (%)	2 (1%)	131 (6%)
Polypharmacy, n (%)	176 (53%)	1191 (56%)
Charlson comorbidity index, median (IQR)	1 (0–2)	-
ADL score, median (IQR)	0 (0–1)	0 (0–1)
IADL score, median (IQR)	1 (0–3)	-

Abbreviations: IQR—Interquartile range; ADL—Activities of Daily Living; IADL—Instrumental Activities of Daily Living

CI 0.11–0.22) in the APOP cohort. Both the measures for expected recovery and adapted ageing showed means close to 0 in both cohorts.

Agreement between the different approaches was poor to moderate (Supplementary Figure 2, Supplementary Table 4). In the TENT cohort, the phenotype approach showed moderate agreement with the expected recovery approach (κ = 0.64, 95% CI 0.57–0.71), while in APOP this agreement was weaker (κ = 0.46, 95% CI 0.43–0.49). The adapted ageing approach showed poor agreement with both the phenotype approach (TENT κ = −0.10, 95% CI −0.16 to −0.03; APOP κ = 0.05, 95% CI 0.03–0.08), and expected recovery approach (TENT κ = 0.15, 95% CI 0.07–0.23; APOP κ = 0.26, 95% CI: 0.23–0.29).

Table 2 presents the discriminative performance of the physical resilience approaches and clinical predictors for 12-month mortality across both cohorts, measured by AUC. In the TENT cohort, the phenotype approach performed best among the physical resilience approaches (AUC 0.69; 95% CI 0.61–0.78), with functional score at follow-up showing comparable performance (AUC 0.68; 95% CI 0.59–0.77). In the APOP cohort, the adapted ageing approach performed best among the physical resilience approaches (AUC 0.61; 95% CI 0.56–0.66), but did not add meaningful discriminative value beyond simpler predictors such as age (AUC 0.65; 95% CI 0.60–0.69) or functional score at follow-up (AUC 0.67; 95% CI 0.63–0.71).

Table 2. Area under the ROC curve for the different predictors of 12-month mortality, stratified by cohort.

	TENT (n = 330)	APOP (n = 2111)
Predictor	AUC (95% CI)	AUC (95% CI)
Phenotype approach	0.69 (0.61–0.78)	0.57 (0.52–0.62)
Expected recovery approach	0.66 (0.56–0.76)	0.57 (0.52–0.63)
Adapted ageing approach	0.55 (0.45–0.64)	0.61 (0.56–0.66)
Age	0.48 (0.39–0.57)	0.65 (0.60–0.69)
Functional score at follow-up[a]	0.68 (0.59–0.77)	0.67 (0.63–0.71)
Geriatric assessment	0.58 (0.50–0.66)	-

[a]IADL at 6 months for the TENT cohort; ADL at 3 months for the APOP cohort

Table 3 presents the discriminative performance of the physical resilience approaches and clinical predictors for the 12-month composite endpoint (decline in quality of life and/or physical functioning, or mortality) across both cohorts, measured by AUC. In both cohorts, the phenotype approach performed best among the physical resilience approaches (TENT AUC 0.62; 95% CI 0.55–0.68; APOP AUC 0.66; 95% CI 0.63–0.68), but did not add meaningful discriminative value beyond simpler predictors such as age (TENT AUC 0.57; 95% CI 0.50–0.65; APOP AUC 0.67; 95% CI 0.64–0.69) or functional status at follow-up (TENT AUC 0.65; 95% CI 0.58–0.71; APOP AUC 0.69; 95% CI 0.66–0.71).

Discussion

In this study, we compared three approaches to estimate physical resilience across two distinct clinical settings in older

Table 3. Area under the ROC curve for the different predictors of 12-month composite endpoint, stratified by cohort.

Predictor	TENT (n = 330) AUC (95% CI)	APOP (n = 2111) AUC (95% CI)
Phenotype approach	0.62 (0.55–0.68)	0.66 (0.63–0.68)
Expected recovery approach	0.61 (0.55–0.68)	0.63 (0.60–0.66)
Adapted ageing approach	0.55 (0.48–0.62)	0.52 (0.49–0.54)
Age	0.57 (0.50–0.65)	0.67 (0.64–0.69)
Functional score at follow-up[a]	0.65 (0.58–0.71)	0.69 (0.66–0.71)
Geriatric assessment	0.53 (0.46–0.6)	-

[a]IADL at 6 months for the TENT cohort; ADL at 3 months for the APOP cohort

adults. We identified two main findings. First, agreement between the approaches on which participants were classified as having high, intermediate or low physical resilience was poor. Second, all three approaches demonstrated only modest discriminative performance for predicting long-term outcomes and did not add predictive value compared to simple clinical predictors such as age and functional status.

Although the application of these different approaches in previous studies [6, 9] have been shown to be associated with clinical outcomes, as far as we know, no studies have assessed the comparative predictive ability of these different approaches within the same cohort. The poor agreement between the different approaches aligns with the earlier findings by Colón-Emeric *et al.* [5] who found that the phenotype approach and expected recovery approach identified different participants as being the most or least physically resilient.

This lack of agreement between the different approaches suggests that these different approaches might not capture the same underlying resilience construct. Residual-based approaches such as expected recovery and adapted ageing may reflect the accuracy of prognostic modelling rather than a patient's physical resilience. In theory, if predictions were perfect, no participant would deviate from the expected trajectory, and physical resilience would not be observed. Therefore, these residual-based approaches seem rather to reflect our ability to predict rather than measuring an underlying characteristic. Conversely, the phenotype approach might not perform adequately enough with only single-timepoint measures of physical functioning. Participants who started and ended at the same level of physical functioning are classified as having equal physical resilience. However, the trajectories of physical functioning for these participants between these measurements might be completely different, something that is not captured by these sparse measurements.

Across both cohorts, all physical resilience approaches demonstrated only modest discriminative ability (AUC 0.5–0.7) for predicting long-term clinical outcomes, and did not add predictive value beyond simpler clinical predictors such as age and functional status. Therefore, in their current form, these approaches are not robust enough to assess physical resilience in patients for clinical practice. Future studies might attempt to more fully capture the dynamic aspect of physical resilience using higher-frequency measurements, such as those from wearable devices.

A strength of this study is the use of two large, well-characterised cohorts representing different clinical contexts, with long-term follow-up and clinically relevant outcomes. Nevertheless, several limitations should be acknowledged. Because two of the three approaches require survival to the follow-up timepoint, patients with the poorest outcomes were not included, potentially biassing the results towards more resilient individuals. Additionally, both cohorts demonstrated relatively preserved pre-stressor function (median ADL 0, IQR 0–1), creating a ceiling effect that limited the potential to detect meaningful differences in physical resilience. Furthermore, heterogeneity in stressor severity (e.g. different chemotherapy regimens or varying severity of acute illness) may have contributed to the modest discriminative performance of all approaches. Additionally, ADL and IADL might not be sensitive enough measures to discriminate between different levels of physical functioning between patients, or measure changes within patients over time. Finally, the time interval between estimating physical resilience and assessing clinical outcomes may have been too long to accurately reflect the dynamic nature of resilience. Shorter follow-up periods may be needed to capture resilience more accurately.

Conclusion

Three different methodological approaches to estimate physical resilience did not agree on which patients classify as having high, intermediate or low physical resilience. The physical resilience approaches did not perform better than simple clinical predictors in discriminative performance for predicting long-term clinical outcomes. The dynamic aspect of physical resilience might not be adequately captured in single-timepoint measurements emphasising the need for higher-frequency assessments to better characterise recovery trajectories.

Supplementary Data: Supplementary data are available at *Age and Ageing* online.

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