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Stage-dependent indirect association between mobility and the cognition-ADL relationship: a cross-sectional study of older adults across the cognitive continuum

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Abstract

Background

Cognitive impairment is a well-established predictor of activities of daily living (ADL) disability. Physical function may serve as an intermediary linking cognitive decline to functional loss, but whether this indirect association differs across the cognitive continuum from normal cognition (NC) to mild cognitive impairment (MCI) to Alzheimer's disease (AD) remains unclear.

Methods

This cross-sectional study included 3,322 community-dwelling older adults (NC: n = 1,234; MCI: n = 814; AD: n = 1,274) from a geriatric clinic in Shanghai, China. Cognitive function was assessed using the Addenbrooke's Cognitive Examination-III. Physical function was measured as grip strength and reverse-transformed Timed Up and Go Test (TUGT; higher values indicate better mobility). Basic and instrumental ADL (BADL and IADL) were reverse-coded so that higher scores indicated better function. Regression-based bootstrap parallel indirect effect analyses (5,000 resamples) were performed in the full sample and within each cognitive stage, adjusting for age, sex, education, and BMI.

Results

Mobility showed a larger absolute indirect effect than grip strength for both BADL (0.015 vs. 0.002) and IADL (0.022 vs. 0.002). The mobility indirect effect increased across cognitive stages for both BADL (NC: 0.003; MCI: 0.005; AD: 0.022) and IADL (NC: 0.004; MCI: 0.008; AD: 0.029). Grip strength was non-significant in MCI and was clearest in AD for BADL. Substantial ADL ceiling effects, especially in NC and MCI, constrain interpretation of stage gradients. Standardized and structural-equation-model sensitivity analyses showed the same mobility-dominant pattern.

Conclusions

In this cross-sectional sample, mobility showed a progressively stronger statistical indirect association with the cognition-ADL relationship as cognitive impairment deepened. The full-sample mobility association persisted after excluding participants with ceiling-level ADL scores. These findings support stage-specific mobility assessment but require longitudinal and experimental confirmation.

Background

Global population aging is accelerating [1]. China is aging especially rapidly: its seventh national population census (2020) recorded 264.02 million people aged 60 years or older (18.70% of the population), including 190.64 million aged 65 years or older (13.50%) [2]. Alzheimer's disease (AD)

affects approximately 55 million people worldwide [3], and in China an estimated 15.07 million adults aged 60 years or older are living with dementia and 38.77 million with mild cognitive impairment (MCI) [4]. MCI, widely recognized as a transitional state between normal cognition and dementia, affects a substantial proportion of older adults [5,6].

A clinically consequential outcome of cognitive decline is deterioration in activities of daily living (ADL), the tasks required for independent living. ADL includes basic ADL (BADL), such as feeding and dressing, and instrumental ADL (IADL), such as shopping and medication management [7,8]. ADL decline contributes to caregiver burden [9,10,11], institutionalization [12], and healthcare costs [13]. In China, where most dementia care is provided by family members, informal caregivers report substantial psychological and physical burden [11], and the annual economic cost of Alzheimer's disease has been estimated at approximately USD 167.7 billion [13].

Longitudinal evidence supports cognition as an important predictor of later functional decline. Sikkes et al. reported that baseline IADL impairment predicted incident dementia over 1–2 years [14]. Sun et al., using cross-lagged panel models, found that cognitive function predicted later-stage ADL loss three years later, whereas the reverse path was not significant [15]. However, the statistical links through which cognitive impairment is associated with ADL disability remain incompletely understood.

Physical function is a plausible intermediary. Individuals with MCI show poorer mobility and balance than cognitively normal peers, including slower gait velocity and shorter stride length [16]. Gait speed under dual-task conditions predicts later functional status [17]. Grip strength also declines along the cognitive continuum and has been linked to cognitive status, amyloid burden, and disability [18–20]. Among functional mobility measures, the Timed Up and Go Test (TUGT) is widely used because it captures an integrated sequence of rising, walking, turning, and sitting that closely overlaps with the task demands of ADL [21]. Shared cognitive-motor neural substrates, including prefrontal cortex, basal ganglia, and hippocampal networks, provide further biological plausibility [22]. The cognitive reserve framework [23] and evidence that functional losses unfold hierarchically as cognitive impairment progresses [24] together suggest that the role of physical function may differ across cognitive stages.

The transition from NC to MCI to AD is characterized by distinct patterns of neural pathology, cognitive reserve, and functional compensation [23,25]. It is therefore unlikely that physical function would have an identical role across stages. BADL and IADL may also differ: IADL tasks often require planning and sequencing, whereas BADL tasks are more directly grounded in physical capacity.

This study examined whether physical function, operationalized as mobility (reverse-transformed TUGT) and grip strength, shows stage-dependent statistical indirect associations with the cognition-ADL relationship across NC, MCI, and AD, and whether these patterns differ between BADL and IADL. We hypothesized that mobility would show stronger indirect associations with ADL than grip strength, and that these associations would be more pronounced in later cognitive stages. Consistent with the cross-sectional design, all results are interpreted as statistical indirect associations rather than as evidence of temporal mediation.

Methods

Study design and participants

This cross-sectional study used data harmonized from two clinical neuropsychological and geriatric assessment databases at the Department of Geriatrics, Shanghai Sixth People's Hospital, Shanghai, China. Of 4,652 participants in the source databases, 3,322 community-dwelling adults aged 60 years or older with complete core data were included. Exclusions were missing cognitive data (n = 487), missing physical function data (n = 341), missing ADL data (n = 286), or exclusion criteria including neurological disorders other than AD, severe psychiatric illness, significant musculoskeletal or cardiovascular conditions precluding physical testing, severe sensory impairment, or inability to complete cognitive testing (n = 216).

Participants were classified by multidisciplinary clinical consensus diagnosis into NC (n = 1,234), MCI (n = 814), and AD (n = 1,274). MCI was diagnosed according to Petersen criteria [5]. AD was diagnosed according to NIA-AA clinical criteria for probable AD dementia [26].

The study was approved by the Ethics Committee of Shanghai Sixth People's Hospital (Approval No. 2016-141-(1)). Written informed consent was obtained from all participants or their legal guardians.

Cognitive assessment

Global cognitive function was assessed using the Addenbrooke's Cognitive Examination-III (ACE-III), a 100-point scale covering attention, memory, verbal fluency, language, and visuospatial ability [27]. ACE-III was selected as the primary cognitive exposure because it provides broader domain coverage than brief screening tools and has demonstrated diagnostic utility for MCI and dementia in Chinese older adults [28]. The Chinese version has demonstrated good reliability in older adults [28]. Recent Chinese studies have further shown that staged screening strategies, informant-based rating scales, and culturally adapted naming tests improve diagnostic precision across the cognitive continuum [29–31].

Physical function assessment

Mobility was assessed using the Timed Up and Go Test (TUGT) [21]. Participants rose from a standard armchair, walked 3 m, turned, returned, and sat down. The average of two trials was used. TUGT was reverse-transformed by multiplying by -1; therefore, higher mobility values indicate better performance throughout the models, tables, and figures.

Grip strength was measured using a Jamar hydraulic hand dynamometer according to a standardized protocol [32]. Three trials were performed alternately on each hand with rest intervals, and the mean across both hands was used.

ADL assessment

Daily function was assessed using a 20-item ADL scale based on Katz BADL and Lawton-Brody IADL constructs [7,8]. Items were originally scored from 1 (independent) to 4 (unable). Scores were reverse-coded so that higher scores indicated better function. BADL comprised 11 items (range 11–44 after reverse coding), and IADL comprised 9 items (range 9–36 after reverse coding). Internal consistency was acceptable for both BADL (alpha = 0.88) and IADL (alpha = 0.82).

Covariates

All models adjusted for age, sex, education, and BMI. These covariates were included on both the cognitive-to-physical-function paths and the physical-function-to-ADL paths.

Statistical analysis

Participant characteristics were summarized by cognitive stage. Group differences were tested using one-way ANOVA for continuous variables and chi-square tests for categorical variables. Effect sizes were reported as eta-squared for ANOVA and Cramer's V for chi-square tests.

Parallel indirect effect analyses were performed using regression-based bootstrap resampling with 5,000 bootstrap samples. ACE-III was specified as the independent variable, grip strength and reverse-transformed TUGT mobility as simultaneous mediators, and BADL or IADL as the outcome. This model estimates the unique statistical indirect effect of each physical-function measure while mutually adjusting for the other mediator; it does not assume that grip strength and mobility are biologically independent. Indirect effects were computed as the product of the a-path and b-path. Confidence intervals were percentile bootstrap 95% intervals; indirect effects were considered statistically significant when the confidence interval excluded zero.

An observed-variable structural equation model (SEM) was fitted as a sensitivity analysis after residualizing all model variables on age, sex, education, and BMI; the grip-strength and mobility residuals were allowed to covary. Fully standardized path coefficients and indirect effects were estimated from the SEM. The bootstrap procedure also included the contrast between the mobility and grip-strength indirect effects, and bootstrap confidence intervals were computed for proportions mediated.

Stage-specific analyses were performed separately within NC, MCI, and AD groups. These are described as stage-comparative analyses because the data are cross-sectional. Sensitivity analyses used sex-stratified models and models excluding participants at the ceiling of each ADL outcome; the ceiling-exclusion analysis was used to evaluate whether the full-sample mobility association was driven by the large number of participants with ceiling-level (fully independent) ADL scores. Full stage-specific a-paths, b-paths, direct effects, total effects, and proportions mediated are reported in Supplementary Table S3; SEM standardized path coefficients, bootstrap contrasts, and bootstrap confidence intervals for proportions mediated are reported in Supplementary Table S5.

All statistical analyses were performed in R (version 4.6.0) using complete-case data. Reporting follows STROBE guidance [33].

Results

Sample characteristics

The final analytical sample included 3,322 participants: 1,234 with NC, 814 with MCI, and 1,274 with AD (Fig. 1). Age increased and education decreased across stages. ACE-III scores, grip strength, mobility, BADL, and IADL all differed significantly across groups (Table 1). Female proportion also differed statistically across groups (p = 0.013), but the effect size was small (Cramer's V = 0.051). Substantial ADL ceiling effects were observed, particularly in NC and MCI (Table 1).

Table 1
Baseline characteristics by cognitive stage

Variable	NC (n = 1,234)	MCI (n = 814)	AD (n = 1,274)	p-value	Effect size
Age, years	68.6 ± 6.0	71.6 ± 7.0	75.0 ± 7.3	< 0.001	0.145
Female, n (%)	790 (64.0)	479 (58.8)	750 (58.9)	0.013	0.051
Education, years	12.1 ± 3.2	11.2 ± 3.7	10.1 ± 4.3	< 0.001	0.052
BMI, kg/m²	23.7 ± 3.2	23.6 ± 3.5	23.0 ± 3.7	< 0.001	0.008
ACE-III	79.1 ± 8.1	68.9 ± 8.7	46.1 ± 14.7	< 0.001	0.630
Grip strength, kg	23.7 ± 7.4	22.0 ± 7.1	19.9 ± 7.1	< 0.001	0.049
TUGT, seconds	9.6 ± 2.6	11.0 ± 3.3	13.5 ± 4.6	< 0.001	0.180
BADL score	43.8 ± 0.8	43.6 ± 1.7	41.9 ± 4.2	< 0.001	0.093
BADL at ceiling, %	92.7	86.2	58.0	-	-
IADL score	35.8 ± 1.1	35.1 ± 2.5	30.5 ± 6.8	< 0.001	0.234
IADL at ceiling, %	92.3	77.0	30.5	-	-

Effect sizes are eta-squared for continuous variables and Cramer's V for sex. BADL and IADL were reverse-coded so that higher scores indicate better function.

Bivariate associations

ACE-III was positively correlated with grip strength (r = 0.308), mobility (r = 0.481), BADL (r = 0.376), and IADL (r = 0.557) (Table 2). Two patterns guided the analyses that follow. First, cognition was more strongly related to mobility (r = 0.481) than to grip strength (r = 0.308). Second, and more importantly, mobility was far more strongly related to ADL than grip strength was: mobility correlated with BADL and IADL at r = 0.402 and r = 0.466, whereas grip strength correlated at only r = 0.149 and r = 0.171. This

asymmetry—similar cognition-to-mediator associations but markedly different mediator-to-ADL associations—motivated the formal indirect-effect decomposition below.

Table 2
Pearson correlations among cognitive function, physical performance, and ADL

Variable	ACE-III	Grip	Mobility	BADL	IADL
ACE-III	1.000				
Grip	0.308	1.000			
Mobility	0.481	0.282	1.000		
BADL	0.376	0.149	0.402	1.000	
IADL	0.557	0.171	0.466	0.788	1.000

All correlations p < 0.001. Higher values indicate better function for all variables; mobility = -TUGT.

Full-sample indirect effects

Because the data are cross-sectional, all indirect effects reported below should be interpreted as statistical indirect associations rather than evidence of temporal mediation.

Each indirect effect is the product of an a-path (cognition to physical function) and a b-path (physical function to ADL), and is expressed as the change in ADL associated with a one-point higher ACE-III score transmitted through that physical-function pathway.

Mobility showed a larger indirect effect than grip strength for both outcomes (Table 3; Fig. 2). For BADL, the mobility indirect effect was 0.015 (95% CI: 0.011, 0.020) and the grip-strength effect was 0.002 (95% CI: 0.001, 0.004). For IADL, the mobility indirect effect was 0.022 (95% CI: 0.017, 0.028) and the grip-strength effect was 0.002 (95% CI: 0.000, 0.005). These values appear small in absolute terms because they represent only the portion of the cognition-ADL association carried by one physical pathway per one-point change in ACE-III. Their importance is better judged by their relative magnitude: mobility accounted for 24.4% of the total ACE-III-BADL association and 13.8% of the total ACE-III-IADL association, whereas grip strength accounted for only 3.5% and 1.5%, respectively. The mobility–grip contrast in indirect effects was 0.013 (95% bootstrap CI: 0.009, 0.018) for BADL and 0.020 (95% bootstrap CI: 0.014, 0.027) for IADL. Bootstrap confidence intervals for proportions mediated were wide, especially for grip strength (BADL: mobility 17.9% to 31.6%, grip 1.4% to 5.9%; IADL: mobility 10.4% to 17.4%, grip 0.1% to 3.0%) (Supplementary Table S5). In the SEM sensitivity analysis, fully standardized indirect effects were 0.084 for mobility and 0.012 for grip with BADL, and 0.072 and 0.008 with IADL (Supplementary Table S5).

Table 3
Full-sample indirect effects

Pathway	Outcome	Indirect effect	95% bootstrap CI	PM
ACE-III -> Grip -> ADL	BADL	0.002	[0.001, 0.004]	3.5%
ACE-III -> Mobility -> ADL	BADL	0.015	[0.011, 0.020]	24.4%
ACE-III -> Grip -> ADL	IADL	0.002	[0.000, 0.005]	1.5%
ACE-III -> Mobility -> ADL	IADL	0.022	[0.017, 0.028]	13.8%

PM, proportion mediated. Models adjusted for age, sex, education, and BMI.

The mobility advantage was driven primarily by the b-path, not the a-path. The cognition-to-mediator paths were similar (ACE-III to grip, a1 = 0.092; ACE-III to mobility, a2 = 0.089), whereas the mediator-to-ADL paths differed substantially: mobility-to-BADL and mobility-to-IADL (b2 = 0.174 and 0.253) were far stronger than grip-to-BADL and grip-to-IADL (b1 = 0.024 and 0.027) (Supplementary Table S1). Thus, although worse cognition was accompanied by both lower grip strength and poorer mobility, only poorer mobility translated strongly into worse ADL.

The BADL and IADL results also merit attention. The absolute mobility indirect effect was larger for IADL (0.022) than BADL (0.015), but its proportion mediated was smaller for IADL (13.8%) than BADL (24.4%), because the total ACE-III-IADL association was much larger than the total ACE-III-BADL association (0.163 vs. 0.063). This contrast is consistent with IADL being more strongly determined by cognition directly, whereas BADL depends relatively more on physical capacity. Full stage-specific direct effects, total effects, and proportions mediated are reported in Supplementary Table S3.

Stage-specific indirect effects

Because the full-sample estimates average across heterogeneous cognitive stages, we next examined whether these indirect associations differed across NC, MCI, and AD.

The mobility indirect effect increased from NC to MCI to AD for both BADL and IADL (Table 4; Fig. 3). For BADL, mobility indirect effects were 0.003 in NC, 0.005 in MCI, and 0.022 in AD. For IADL, corresponding values were 0.004, 0.008, and 0.029.

Table 4
Stage-specific indirect effects

Pathway	NC	MCI	AD
Mobility -> BADL	0.003 [0.001, 0.006]	0.005 [0.001, 0.009]	0.022 [0.014, 0.030]
Mobility -> IADL	0.004 [0.001, 0.007]	0.008 [0.003, 0.016]	0.029 [0.019, 0.040]
Grip -> BADL	0.001 [0.000, 0.001]	0.000 [-0.002, 0.002]	0.005 [0.002, 0.008]
Grip -> IADL	0.001 [0.000, 0.002]	0.002 [-0.001, 0.005]	0.005 [-0.000, 0.010]

Values are indirect effect [95% bootstrap CI]. Models adjusted for age, sex, education, and BMI.

The grip-strength results showed a different pattern. Grip effects were very small in NC, non-significant in MCI, and clearest in AD for BADL. In AD, the grip-BADL indirect effect was 0.005 (95% CI: 0.002, 0.008), whereas the grip-IADL confidence interval crossed zero slightly (0.005; 95% CI: -0.000, 0.010).

Sensitivity analyses

We then tested the robustness of these patterns. Sex-stratified analyses preserved the mobility-dominant pattern, although grip-strength effects were less consistent, particularly among men (Supplementary Table S2). The SEM sensitivity analysis and fully standardized estimates likewise preserved the mobility-dominant pattern (Supplementary Table S5).

After excluding participants at the ceiling of each ADL outcome, the full-sample mobility indirect association remained significant for BADL (n = 737; IE = 0.012; 95% CI: 0.006, 0.020) and IADL (n = 1,167; IE = 0.019; 95% CI: 0.012, 0.028). Grip-strength indirect associations were no longer significant. Stage-specific non-ceiling analyses were unstable in NC and MCI because the remaining samples were small (BADL: n = 90 and 112; IADL: n = 95 and 187), supporting caution in interpreting early-stage gradient estimates (Supplementary Table S4).

Discussion

This cross-sectional study found that mobility showed a larger and more stage-dependent statistical indirect association with the cognition-ADL relationship than grip strength. The mobility indirect association was present across all cognitive stages and increased from NC to MCI to AD, whereas grip-strength effects were small in NC, absent in MCI, and most evident in AD for BADL. These findings suggest that the physical-function component of the cognition-ADL relationship is not uniform across the cognitive continuum. Rather, mobility may become increasingly relevant as cognitive impairment deepens and functional reserve is progressively reduced.

This pattern is consistent with three complementary frameworks. First, the cognitive reserve framework [23] predicts that preserved compensatory capacity buffers the functional impact of early motor limitations, so physical-function effects become visible only as reserve is progressively exhausted,

matching the observed NC-to-MCI-to-AD gradient. Second, the shared cognitive-motor decline concept [22,34,35] proposes that cognition and mobility rely on overlapping prefrontal, basal ganglia, and hippocampal circuits, so cognitive impairment progressively weakens the very motor processes needed for independent ADL. Third, evidence on the hierarchical loss of function [15,24,37] indicates that functional decline unfolds progressively and becomes more evident as cognitive impairment deepens. These frameworks therefore converge on the same expectation: physical function, especially mobility, should be most consequential in later cognitive stages.

These findings are consistent with recent mediation evidence in older adults with dementia. Barros et al. reported that physical fitness (lower-body strength, aerobic capacity, and mobility) significantly mediated the association between basic ADL independence and quality of life (standardized indirect effect β = 0.242), whereas cognitive function did not [39]. Longitudinal evidence from CHARLS likewise indicates that physical function limitation, depression, and cognitive deficits jointly contribute to incident ADL disability [40]. Recent structural equation modelling in Chinese older adults has further shown that daily living ability and sleep mediate the depression–cognition relationship [41]. The present study extends that work by showing that mobility is a more consistent physical-function mediator than grip strength across the cognitive continuum, and that this indirect association is most pronounced in AD. Methodologically, Barros et al. used latent physical-fitness and cognitive-function factors within an SEM; our SEM sensitivity analysis, although based on observed variables, produced the same mobility-dominant pattern, supporting the robustness of the bootstrap estimates.

Mobility as the stronger physical-function correlate

The most consistent result was the dominance of mobility over grip strength. This difference was not primarily driven by stronger associations between cognition and mobility than between cognition and grip; the cognitive-to-mediator paths were similar. Instead, mobility had a much stronger association with ADL after accounting for cognition and grip strength.

This divergence can be understood from the different constructs that the two measures capture. In the present study, mobility was operationalized as the reverse-transformed TUGT [21], which requires the integrated sequencing of rising, walking, turning, and sitting, tasks that depend on attention, executive control, dynamic balance, and motor planning and that closely overlap with ADL activities such as transferring, toileting, ambulation, shopping, and community mobility. Grip strength, by contrast, is a maximal hand-grip measure that primarily reflects muscle mass and peripheral neuromuscular function, involves minimal cognitive control, and maps onto a narrower set of task demands [19,20]. This distinction is consistent with prior work showing that functional mobility measures are more strongly associated with ADL disability, falls, and adverse outcomes than strength measures [34,36], whereas grip strength is most closely linked to sarcopenia, frailty, and overall physiological reserve [19,20]. Thus, mobility may capture the point at which cognitive decline begins to affect the coordinated, cognitively demanding motor performance required for daily independence, whereas grip strength may remain a more general marker of bodily reserve.

The finding also aligns with geriatric evidence that mobility and gait performance are powerful indicators of later adverse outcomes. Gait speed has been described as a global marker of health and survival in older adults [34], and physical performance measures add prognostic information beyond conventional clinical characteristics [36]. More recently, exceptionally fast gait speed in adults aged 80 years or older has been associated with slower cognitive aging and preserved hippocampal subfield volumes, suggesting that mobility may index cognitive and brain reserve [42]. In cognitive aging, mobility impairment may be especially informative because walking is not a purely motor task: it requires attention, executive control, visuospatial processing, and motor planning [22,35].

Stage-dependent pattern and ceiling effects

The increasing mobility indirect effect from NC to MCI to AD is consistent with a stage-dependent amplification pattern. One possible interpretation is that, in cognitively normal older adults, cognitive reserve and preserved compensatory capacity buffer the impact of mild mobility limitations on daily function [23]. In MCI, this buffer may weaken: subtle executive and attentional deficits can make mobility problems more consequential for complex daily activities, particularly IADL. In AD, the combination of cognitive impairment, poorer motor planning, reduced activity, and frailty may make mobility a more direct constraint on both BADL and IADL. Prior work showing linked motor and cognitive trajectories before dementia supports this general interpretation [35], and evidence on the hierarchical loss of ADL suggests that functional decline becomes more visible as cognitive impairment deepens [15,24,37].

The ceiling-effect sensitivity analysis provides an important qualification. Substantial ADL ceiling effects were observed (BADL: 92.7% in NC, 86.2% in MCI, and 58.0% in AD; IADL: 92.3%, 77.0%, and 30.5%, respectively), which restricted variance in the early stages. After removing participants with ceiling-level ADL scores, the full-sample mobility association remained statistically evident for both BADL and IADL, indicating that the mobility finding is not solely an artifact of the large number of fully independent participants. The same analysis also showed why early-stage subgroup estimates should be treated cautiously: only 90 NC and 112 MCI participants remained for BADL, and only 95 NC and 187 MCI participants remained for IADL. These small non-ceiling samples produced unstable subgroup estimates. Therefore, the stronger AD-stage mobility association is unlikely to be explained entirely by ceiling effects, but the apparent NC-to-MCI-to-AD gradient should still be interpreted as a stage-comparative pattern rather than a confirmed biological progression.

The stage gradient should not be interpreted as proof of temporal mediation. The study is cross-sectional, and the ADL measures showed substantial ceiling effects, particularly in NC and MCI. The higher indirect effects observed in AD may therefore reflect both genuine clinical amplification and greater measurable variance in ADL. Future work should test this pattern using longitudinal or cross-lagged models with repeated measures of cognition, mobility, and ADL.

Grip strength

Grip-strength indirect effects were less consistent. The NC estimates were very small, MCI effects were non-significant, and the clearest signal appeared in AD for BADL. This pattern is compatible with, but does not confirm, a threshold interpretation: grip strength may become functionally consequential only after it falls below levels at which everyday manipulation, transfers, or self-care tasks are affected. Consensus definitions of sarcopenia emphasize low muscle strength as a central feature of impaired physical capability [19], and epidemiological work links weak grip strength to disability, morbidity, and mortality [20]. In the present sample, mean grip strength was lowest in AD, making it more likely that strength deficits had reached a functionally meaningful range.

At the same time, the weaker grip association should not be read as evidence that muscle strength is unimportant. Grip strength may represent global physiological reserve rather than the specific task sequence required for ADL performance. It may also interact with sex, body size, nutrition, and comorbidity. The sex-stratified sensitivity analyses support this caution: mobility remained robust across strata, whereas grip-related effects were less stable. Clinically, this suggests that grip strength is useful as a screening marker, but mobility assessment may be more directly informative when the goal is to understand cognition-related ADL vulnerability.

BADL and IADL differences

The BADL and IADL findings also deserve separate interpretation. IADL is often affected earlier in cognitive disorders because tasks such as medication management, finances, transportation, and shopping require planning, sequencing, working memory, and environmental problem solving [8,14,15]. BADL tends to be preserved until later stages, but when BADL impairment emerges it is closely tied to basic physical capacities such as transfer ability, balance, and ambulation [7,24]. In this study, mobility was relevant to both domains, but the clinical meaning differs. For IADL, mobility may enable participation in cognitively demanding community tasks; for BADL, mobility may be closer to the immediate physical substrate of independence. This distinction helps explain why mobility can be a shared pathway across domains while the remaining direct cognition-ADL association remains particularly important for IADL.

Clinical implications

These findings support routine mobility assessment across the cognitive continuum, particularly in MCI and AD. The result is consistent with integrated geriatric-care approaches that prioritize intrinsic capacity, mobility, and function rather than cognition alone [38]. In practical terms, TUGT or related mobility tests may help identify older adults whose cognitive impairment is already accompanied by physical vulnerability relevant to ADL. Such assessment is brief, inexpensive, and feasible in outpatient geriatric settings.

Mobility is a trainable capacity: gait, balance, transfer, and task-specific exercise can improve TUGT performance, and the estimated b-paths indicated that a one-second faster TUGT was associated with 0.17-point and 0.25-point higher BADL and IADL scores, respectively. These cross-sectional associations

therefore identify mobility as a plausible, modifiable intervention target, but they cannot establish that improving mobility would improve ADL; that requires prospective intervention trials.

The findings also suggest that mobility-focused interventions may be especially relevant in MCI, where ADL impairment is not yet advanced but the mobility-ADL statistical association has begun to strengthen. This does not mean that mobility training can be assumed to prevent disability; the present data cannot establish intervention effects. Rather, the results provide a rationale for trials that combine cognitive assessment with mobility, balance, transfer, and gait interventions, and that include ADL outcomes as endpoints. In AD, mobility assessment may remain important for care planning, fall prevention, caregiver education, and environmental modification, even if reversal of established functional loss is less likely.

Strengths and limitations

Strengths include the large clinical sample, inclusion of NC, MCI, and AD groups, parallel comparison of grip strength and mobility, separate BADL and IADL outcomes, and bootstrap estimation of indirect effects.

Several limitations should be noted. First, the cross-sectional design precludes causal inference; reverse and reciprocal associations are plausible, because ADL restriction may reduce physical activity and social participation and thereby worsen mobility. Second, the single-center urban clinical sample may limit generalizability to rural populations or other healthcare systems. Third, physical function was represented by TUGT and grip strength only; more detailed measures, such as gait speed, dual-task gait, balance, lower-extremity strength, and the Short Physical Performance Battery, may identify more specific motor associations [16,22,35]. These single-task indicators are observed variables that may contain measurement error; the SEM sensitivity analysis modeled residual covariation between grip strength and mobility but could not separate a broader latent physical-function construct. Fourth, clinical diagnostic categories may contain heterogeneity, particularly within MCI, where etiologies and progression risks vary [5,6]. Finally, residual confounding remains possible because physical activity, depression, nutrition, comorbid disease, vascular burden, medication burden, and social support were not fully measured in the primary models. Substantial ADL ceiling effects limited early-stage subgroup estimates, but the full-sample mobility association remained robust after excluding ceiling-level participants, supporting the stability of the main finding.

Future studies should use longitudinal multi-wave designs to test whether worsening cognition precedes mobility decline and whether mobility decline subsequently predicts ADL loss. Studies with performance-based ADL measures or item-response-theory-scaled ADL instruments would help address ceiling effects. Neuroimaging or biomarker-informed designs could also clarify whether the observed mobility association reflects Alzheimer's pathology, vascular burden, sarcopenia, or shared multisystem aging.

Conclusions

Mobility showed a stronger statistical indirect association than grip strength with the cognition-ADL relationship, and this association increased across the cognitive continuum from NC to MCI to AD. Because the study is cross-sectional and ADL ceiling effects were substantial, the stage-gradient pattern should be interpreted cautiously. These findings support stage-specific mobility assessment in older adults with cognitive impairment. Longitudinal and experimental studies are needed to confirm causal mechanisms and intervention effects.

Abbreviations

AD
Alzheimer's disease
ACE-III
Addenbrooke's Cognitive Examination-III
ADL
Activities of daily living
BADL
Basic activities of daily living
BMI
Body mass index
CI
Confidence interval
IADL
Instrumental activities of daily living
MCI
Mild cognitive impairment
NC
Normal cognition
PM
Proportion mediated
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
TUGT
Timed Up and Go Test

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Ethics Committee of Shanghai Sixth People's Hospital (Approval No. 2016-141-(1)). Written informed consent was obtained from all participants or their legal guardians.

Clinical trial number

Clinical trial number: not applicable.

Use of assessment instruments

This study did not use the Morisky Medication Adherence Scale (MMAS-8) or any other medication adherence scale. Cognitive and physical function were assessed with the Addenbrooke's Cognitive Examination-III (ACE-III), Timed Up and Go Test (TUGT), Jamar hand dynamometer, and a 20-item ADL scale based on the Katz and Lawton-Brody indices. The ACE-III was administered as part of routine clinical assessment at Shanghai Sixth People's Hospital. The TUGT is a performance-based mobility test and the Jamar hand dynamometer is a measurement device; neither involves copyrighted questionnaire content. The 20-item ADL scale was based on published Katz and Lawton-Brody constructs. No ACE-III items, scoring content, or other copyrighted scale items are reproduced in this manuscript or its supplementary materials.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study and the analysis code are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Z.W., Y.X., and Q.G. conceived and designed the study. Z.W. performed the statistical analyses and drafted the manuscript. H.X., Y.P., and Z.X. contributed to data acquisition, data curation, and clinical assessments. Y.X. and Q.G. supervised the study and are the corresponding authors. Y.X., Q.G., and H.X.

contributed to the interpretation of the results and critically revised the manuscript. All authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

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Figures

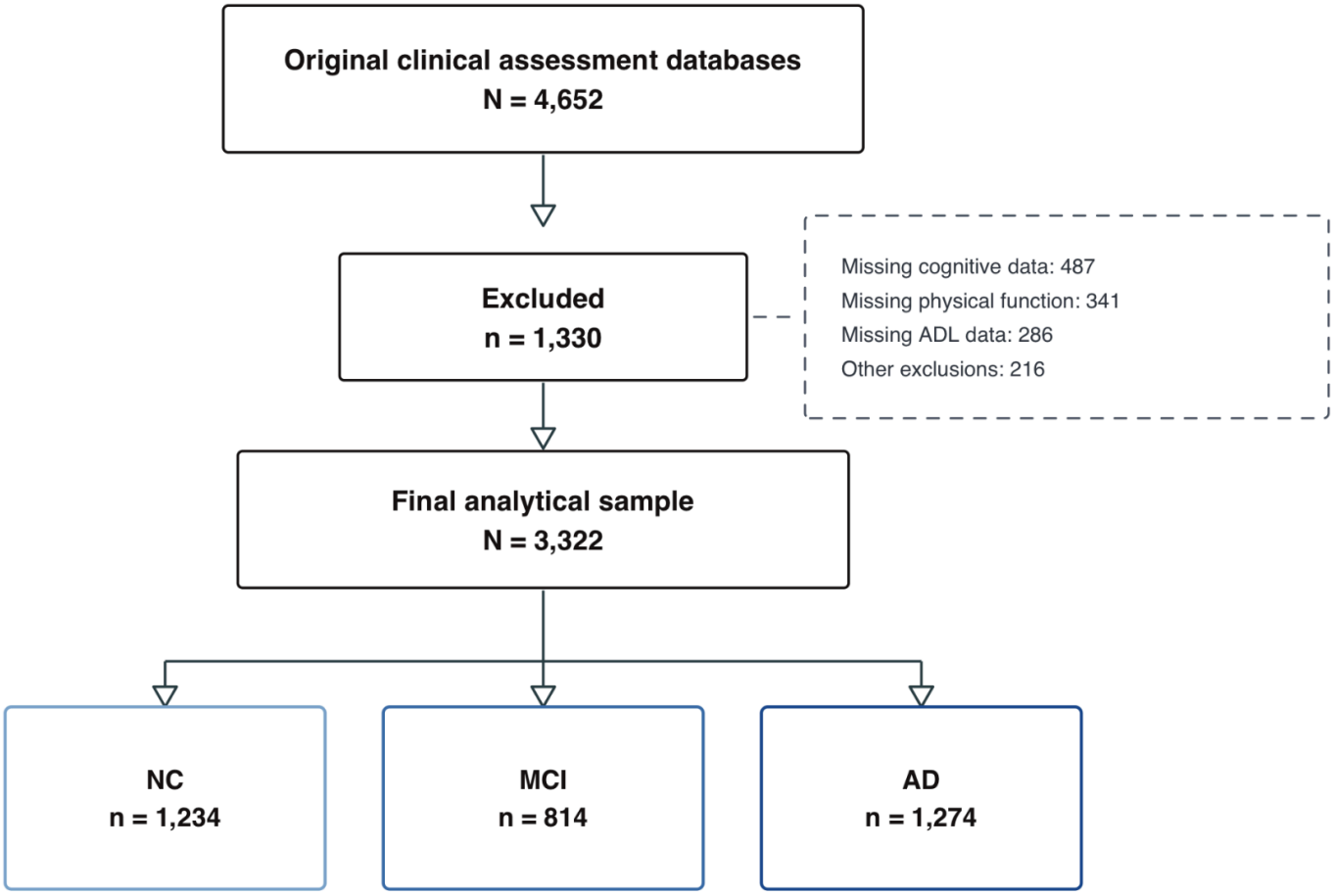
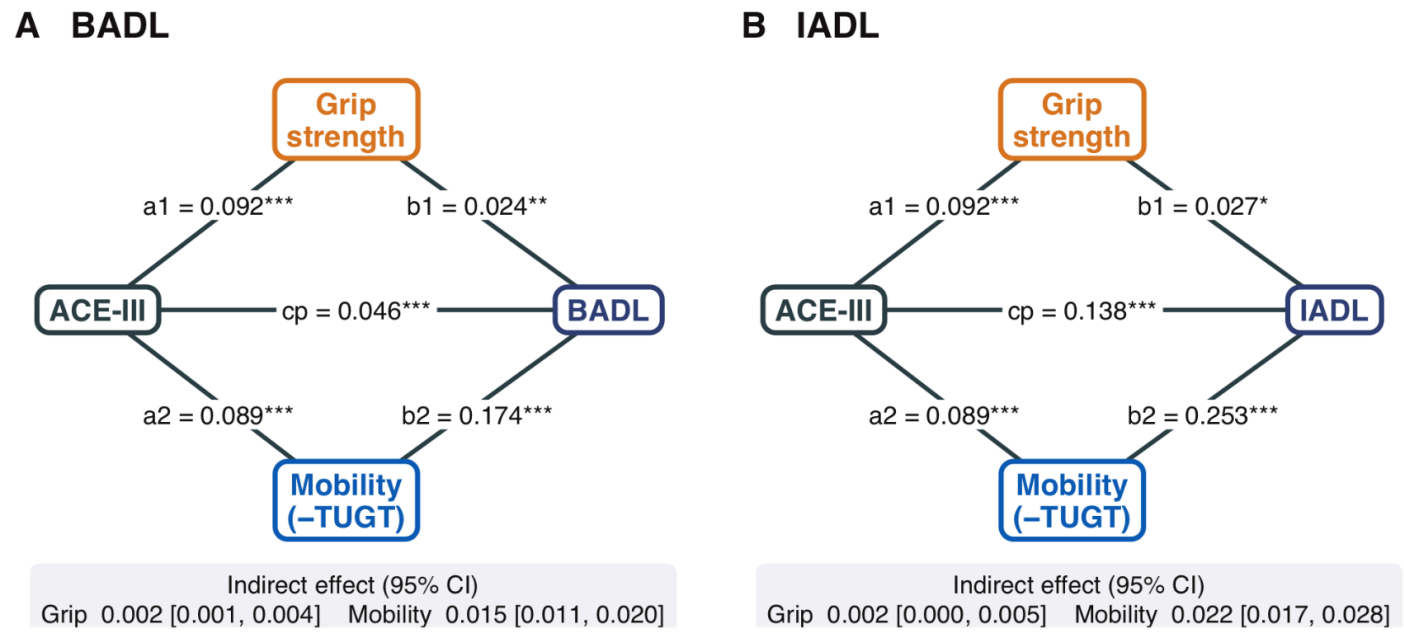


Figure 1

Participant flow. STROBE flow diagram of participant inclusion and exclusion.



Adjusted for age, sex, education, and BMI. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Figure 2

Path diagrams. Parallel indirect effect path diagrams for BADL and IADL in the full sample. Values are unstandardized coefficients with * $p < 0.05$, **$p < 0.01$,** * $p < 0.001$. Models adjusted for age, sex, education, and BMI.

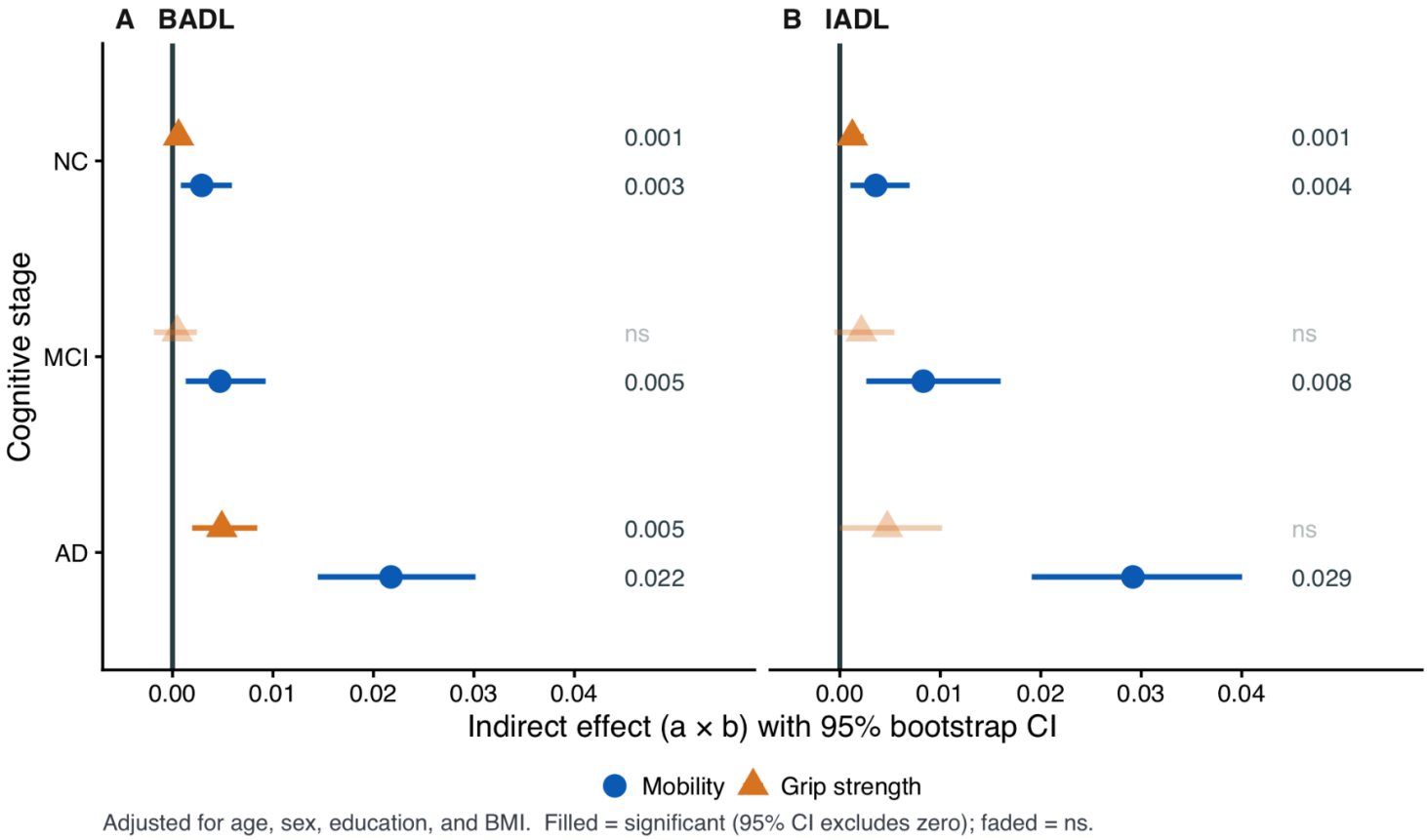


Figure 3

Stage-specific indirect effects. Indirect effects across NC, MCI, and AD for mobility and grip-strength models. Points represent unstandardized indirect effects; bars indicate 95% bootstrap confidence intervals. Filled symbols indicate that the 95% CI excludes zero; faded symbols indicate non-significant estimates.

Supplementary Files

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- SupplementaryTablesS1S5.xlsx