Protocol

Official Title: Effects of resistance-based exercise snacks with varying fragmentation patterns on lower limb function and executive cognition in pre-frail older adults

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1. ABSTRACT

Background: Exercise snacks have emerged as a promising strategy to improve physical function in older adults. However, the optimal fragmentation pattern (i.e., how to distribute a fixed daily volume of exercise across the day) remains unknown. Furthermore, the effects of resistance-based exercise snacks on cognitive function in pre-frail older adults have not been investigated.

Objective: To compare the effects of four different fragmentation patterns of a three-exercise resistance snack (sit-to-stand, squat, and heel raise) on lower limb strength, dynamic balance, and executive cognitive function in community-dwelling pre-frail older adults.

Design: Four-arm parallel-group randomized controlled pilot trial.

Participants: 60 community-dwelling pre-frail older adults (Fried Frailty Phenotype score 1-2, aged ⩾65 years).

Interventions: All groups perform a fixed total daily volume of 15 repetitions per exercise (sit-to-stand, squat, and heel raise), resulting in 45 total repetitions per day. The only difference between groups is the fragmentation pattern:

- G1 (highly fragmented): 1 repetition of each exercise per bout, 15 bouts/day (~30 seconds per bout)
- G2 (moderately fragmented): 3 repetitions of each exercise per bout, 5 bouts/day (~90 seconds per bout)
- G3 (lowly fragmented): 5 repetitions of each exercise per bout, 3 bouts/day

(~2.5 minutes per bout)

- G4 (consecutive control): 15 repetitions of each exercise per bout, 1 bout/day (~7.5 minutes per bout)

The intervention period is 8 weeks.

Outcome Measures: Primary outcomes include lower limb strength (30-second chair stand test) and dynamic balance (Timed Up and Go test). Secondary outcomes include comprehensive physical function (Short Physical Performance Battery), executive function (Stroop Color-Word Test and Trail Making Test), and falls efficacy (modified Falls Efficacy Scale). Feasibility outcomes include adherence, acceptability, and adverse events.

Data Analysis: A 4 × 3 mixed ANOVA will be used to compare group differences. Effect sizes (Cohen's d, η^2) will be estimated to inform a future definitive randomized controlled trial.

Expected Results: This pilot trial will provide preliminary evidence on the dose-response relationship between exercise snack fragmentation patterns and both physical and cognitive outcomes in pre-frail older adults.

2. INTRODUCTION AND BACKGROUND

2.1 Definition and Epidemiology of Pre-Frailty

Frailty is a geriatric syndrome characterized by multisystem dysregulation leading to reduced physiological reserve and increased vulnerability to stressors. The Fried Frailty Phenotype classifies individuals into three categories: robust (0 criteria), pre-frail (1-2 criteria), and frail (⩾3 criteria). Pre-frailty is an intermediate state between health and frailty and is potentially reversible.

The prevalence of pre-frailty among community-dwelling older adults in China ranges from 26.8% to 62.8%. Pre-frailty represents a "golden window" for intervention because early identification and targeted intervention can reverse pre-frailty to a robust state or delay its progression to frailty.

2.2 Three Types of Exercise Snacks

According to a 2024 scoping review published in *Sports Medicine*, exercise snacks are classified into three types:

Type	Definition	Characteristics
Structured Exercise Snacking	Planned, short bouts of structured exercise	<5 minutes per bout, ≥2 bouts per day
Snacktivity	Activity pattern aimed at frequently breaking up sedentary time	2-5 minutes, multiple times per day
VILPA	High-intensity activities occurring naturally in daily life	1-2 minutes, vigorous intensity

VILPA requires vigorous intensity and is not suitable for pre-frail older adults due to safety concerns. This study focuses on the structured exercise snacking paradigm while incorporating Snacktivity logic (high-frequency interruption of sedentary behavior) as a theoretical comparator.

2.3 Research Gaps

Although exercise snacks have been demonstrated to be feasible in older adults (adherence rates 81-97%), several research gaps remain:

1. **Optimal dose unknown:** No study has systematically compared different fragmentation patterns
2. **Cognitive effects unexplored:** The effects of exercise snacks on cognitive function have not been investigated
3. **Limited resistance-based evidence:** Existing cognitive studies have exclusively used aerobic-based exercise snacks

2.4 Study Objectives

This study aims to:

1. Compare the effects of four different fragmentation patterns on lower limb function and executive cognitive function in pre-frail older adults
2. Explore the dose-response relationship between fragmentation pattern and intervention effects
3. Determine whether 15 repetitions per day is above, at, or below the minimal effective dose threshold for resistance-based exercise snacks

3. STUDY DESIGN

Design Overview

- **Design:** Four-arm parallel-group randomized controlled pilot trial

- **Allocation Ratio:** 1:1:1:1
- **Masking:** Assessor-blind (outcome assessors unaware of group assignment)
- **Intervention Period:** 8 weeks
- **Assessment Time Points:** Baseline (Week 0), Mid-intervention (Week 4), Post-intervention (Week 8)

4. STUDY POPULATION

4.1 Inclusion Criteria

1. Age 65 years or older
2. Community-dwelling (living independently, not in a nursing home or long-term care facility)
3. Pre-frail status confirmed by Fried Frailty Phenotype score of 1-2
4. Mini-Mental State Examination (MMSE) score ⩾24
5. Able to walk independently with or without a cane
6. No regular lower limb strength training (less than 2 times per week) in the past 3 months
7. Willing to adhere to the 8-week exercise intervention and complete all assessments
8. Provide written informed consent before any study-related procedures

4.2 Exclusion Criteria

1. Lower limb fracture or joint replacement surgery within the past 6 months
2. Unstable angina or uncontrolled hypertension (resting systolic blood pressure ⩾160 mmHg)
3. Severe osteoporosis (T-score < -2.5 with history of fragility fracture)
4. Neurological disorders affecting motor function (e.g., Parkinson's disease, post-stroke hemiplegia)
5. Severe cognitive impairment (MMSE score <24)
6. Unstable cardiac or pulmonary disease (e.g., recent myocardial infarction, severe COPD exacerbation)
7. Severe visual or hearing impairment that limits ability to follow instructions or

perform exercises safely

8. Participation in another interventional clinical trial within the past 30 days
9. Any other medical or psychological condition that, in the opinion of the principal investigator, would compromise participant safety or study adherence

4.3 Sample Size

As a pilot trial, formal power calculation is not performed. Fifteen participants per group (total N=60) will be recruited. Anticipating a 20-25% attrition rate, approximately 45 participants (11-12 per group) are expected to complete the 8-week intervention.

5. INTERVENTION

5.1 Four-Group Design Overview

All groups perform a fixed total daily volume of 15 repetitions per exercise (sit-to-stand, squat, and heel raise), resulting in 45 total repetitions per day. The only difference between groups is the fragmentation pattern.

Group	Repetitions per Bout (per exercise)	Bouts per Day	Duration per Bout	Fragmentation Level
G1 (Highly Fragmented)	1	15	~30 seconds	Highest
G2 (Moderately Fragmented)	3	5	~90 seconds	Moderate
G3 (Lowly Fragmented)	5	3	~2.5 minutes	Lower
G4 (Consecutive Control)	15	1	~7.5 minutes	None

5.2 Exercise Standardization

Sit-to-Stand:

- Starting position: Seated on a rigid chair (seat height 43-45 cm), feet shoulder-width apart, hands crossed over chest
- Movement: Lean forward → extend knees to stand → hold fully upright for 1 second → slowly sit back down
- Progression/regression: Hands on armrests (regression), seat height increase (regression)

Squat:

- Starting position: Standing, feet shoulder-width apart, hands on hips or holding chair back
- Movement: Keep back straight → bend knees and lower hips as if sitting back → thighs parallel to ground → stand up

- Progression/regression: Partial squat (regression), holding chair back (regression)

Heel Raise:

- Starting position: Standing, feet together, hands lightly holding chair back for balance
- Movement: Slowly raise heels to maximum height → hold for 1 second → slowly lower
- Progression/regression: Holding chair back with both hands (regression)

5.3 Triggering Strategies

Group	Trigger Type	Specific Instructions
G1	Event-based	Perform one bout after each bathroom visit and after each time drinking water
G2	Fixed time points	Perform bouts at approximately 9:00, 12:00, 15:00, 18:00, and 21:00
G3	Fixed time points	Perform bouts at morning (9:00), noon (14:00), and evening (19:00)
G4	Fixed time	Perform the single daily bout at a consistent time (e.g., 10:00 AM)

5.4 Progressive Loading

Phase	Weeks	Strategy
Adaptation	1-2	Slow controlled speed, emphasis on movement quality
Stabilization	3-5	Moderate speed, increase repetitions per bout for G2 and G3
Progression	6-8	Explosive speed (sit-to-stand and squat), optional weighted vest (2-4 kg) for G3 and G4

6. OUTCOME MEASURES

6.1 Primary Outcome Measures

Outcome	Measure	Time Points
Lower Limb Muscle Strength	30-Second Chair Stand Test (30-CST). Number of complete sit-to-stand repetitions within 30 seconds. Higher score indicates better strength.	Baseline, Week 4, Week 8
Dynamic Balance and Mobility	Timed Up and Go (TUG) test. Time (seconds) to stand from a chair, walk 3 meters, turn, walk back, and sit down. Shorter time indicates better balance and mobility.	Baseline, Week 4, Week 8

6.2 Secondary Outcome Measures

Outcome	Measure	Time Points
Comprehensive Physical Function	Short Physical Performance Battery (SPPB). Composite score (0-12) based on standing balance (0-4), 4-meter gait speed (0-4), and 5-repetition chair stand time (0-4). Higher score indicates better function.	Baseline, Week 4, Week 8
Executive Function - Inhibition Control	Stroop Color-Word Test (SCW). Three parts: Word, Color, and Color-Word. Interference effect (SCW score ÷ Color score) is calculated. Lower values indicate better inhibition control.	Baseline, Week 4, Week 8
Executive Function - Cognitive Flexibility	Trail Making Test (TMT). TMT-A (numbers 1-25) and TMT-B (alternating numbers and letters). Difference (TMT-B minus TMT-A) is calculated. Smaller differences indicate better cognitive flexibility.	Baseline, Week 4, Week 8
Falls Efficacy	Modified Falls Efficacy Scale (FES). 16-item questionnaire (0-10 per item, total 0-160). Higher scores indicate better falls efficacy.	Baseline, Week 8

6.3 Feasibility Outcomes

Outcome	Definition	Success Criterion
Recruitment Rate	(Number randomized ÷ Number screened eligible) × 100%	≥60%
Retention Rate	(Number completed 8 weeks ÷ Number randomized) × 100%	≥80%
Adherence	(Actual bouts completed ÷ Prescribed bouts) × 100%	≥80%
Acceptability	5-point Likert scale questionnaire	Mean score ≥4
Safety	Adverse event rate	No serious adverse events

8. RANDOMIZATION AND BLINDING

8.1 Randomization

- **Method:** Online random number generator (Sealed Envelope)
- **Allocation Ratio:** 1:1:1:1
- **Stratification Factors:** Sex, baseline SPPB score (3-6 vs. 7-10)

- ### 8.2 Blinding

Role	Blinded?
Participants	No
Intervention Providers	Yes
Outcome Assessors	Yes
Data Analysts	Yes

9. DATA COLLECTION AND MANAGEMENT

9.1 Data Collection Tools

- **Physical function tests:** 30-second chair stand test, TUG, SPPB
- **Cognitive tests:** Stroop Color-Word Test, Trail Making Test
- **Questionnaires:** FES, IPAQ, Acceptability Questionnaire

- **Process monitoring:** Exercise log, Borg CR-10 scale, video 抽查

9.2 Data Management

- Electronic data capture system (e.g., REDCap)
- Double data entry with cross-verification
- Data stored on encrypted servers

10. STATISTICAL ANALYSIS

10.1 Analysis Populations

Population	Definition	Purpose
ITT (Intention-to-Treat)	All randomized participants, analyzed according to original group assignment	Primary analysis
PP (Per-Protocol)	Participants with adherence ≥80%	Sensitivity analysis
Safety Population	Participants who received at least one intervention session	Adverse event analysis

10.2 Statistical Methods

Analysis Purpose	Statistical Method
Baseline characteristics comparison	One-way ANOVA or chi-square test
Within-group changes	Paired t-test or Wilcoxon signed-rank test
Between-group differences	4 × 3 mixed ANOVA, post-hoc Tukey HSD
Trend analysis	Polynomial contrast (linear, quadratic)
Effect sizes	Cohen's d (within-group), η^2 (between-group)

10.3 Missing Data Handling

- Multiple imputation (5 imputations) for random missing data
- Sensitivity analysis comparing ITT and PP results

10.4 Sample Size Justification

As a pilot trial, formal power calculation is not performed. Fifteen participants per group (total N=60) will allow estimation of effect sizes (width of 95% CI for Cohen's d) and feasibility outcomes (recruitment, retention, adherence).

11. SAFETY

11.1 Adverse Event Monitoring

Event Type	Definition	Management
Fall	Unexpected contact with ground	Assess cause, modify protocol
Muscle strain	Persistent pain >24 hours post-exercise	Rest, heat therapy
Joint pain	Sharp pain in knee/hip joint	Stop exercise, assess movement
Dizziness	Lightheadedness post-exercise	Rest, monitor blood pressure

11.2 Early Termination Criteria

- One or more serious adverse events occur
- Attrition rate >40% in any group
- Participant voluntarily withdraws

12. ETHICAL CONSIDERATIONS

12.1 Ethical Approval

- The protocol has been reviewed and approved by the Institutional Review Board of [Institution Name]
- Approval number: [To be filled]
- Approval date: [To be filled]

12.2 Informed Consent

- All participants will provide written informed consent
- The informed consent form includes: study purpose, procedures, risks, benefits, confidentiality, and voluntary withdrawal

12.3 Data Confidentiality

- Participant data will be anonymized
- Only the research team will have access to raw data

12.4 Clinical Trial Registration

- This study is registered at ClinicalTrials.gov
- NCT number: [To be assigned]

13. REFERENCES

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4. Perkin et al. (2019). Exercise snacks in older adults. *Journal of Aging Research*.
5. Chinese Clinical Practice Guidelines for Exercise Intervention in Frail Older Adults (2025).