Accelerometer-Measured Physical Activity Improves Predictive Validity of Fried Frailty Phenotype for All-Cause and Cardiovascular Disease Mortality: UK Biobank

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INTRODUCTION

- Frailty is a significant health challenge among older adults, increasing vulnerability to adverse health outcomes such as cardiovascular disease (CVD), falls, disability, and mortality.[1]
- Fried Frailty Phenotype (FFP) is a widely used frailty measure defined by five criteria: unintentional weight loss, exhaustion, slowness, weakness, and low physical activity (PA). [2]
- Low PA is typically assessed by self-report, which is less accurate than accelerometer-based measures - particularly in older adults.[3]
- This study examined whether replacing self-reported PA with accelerometer-measured PA improves the predictive validity of the FFP for all-cause and CVD mortality.

HYPOTHESES

- Frail and pre-frail older adults have higher risks of all-cause and CVD mortality than robust individuals.
- The FFP incorporating accelerometer-measured PA shows stronger associations with mortality than the FFP incorporating self-reported PA.

METHODS

- **Study Design:** Prospective cohort study.
- **Participants:** 38,429 UK Biobank participants aged ≥ 60 years.[4]
- **Accelerometer Assessment:**
  - Axivity AX3 on the dominant wrist for 7 days, 24 hours/day (Figure 1).[4]
  - <3 valid wear days or lacking hourly acceleration data were excluded.[4]
- **Frailty Assessment:** Frailty was defined using the 5 modified FFP criteria adapted for UK Biobank (Figure 2).[5] Frailty status was classified as robust (0 criteria), pre-frail (1–2), or frail (≥3).[5]
  - **FFP-Mod:** Low PA assessed using self-reported PA.[5]
  - **FFP-MVPA:** Low PA defined as the lowest quintile of time spent at acceleration >125 mg based on acceleration intensity distribution.

Figure 1. Axivity AX3 Accelerometers

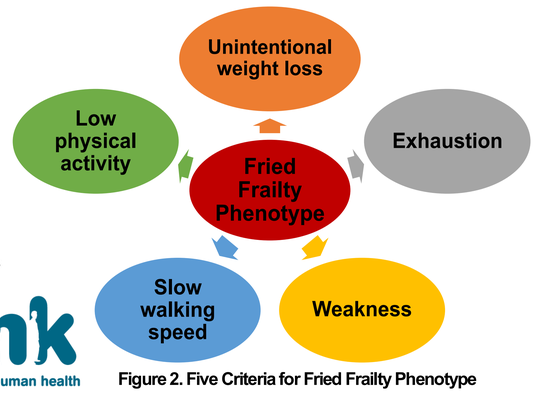


Figure 2. Five Criteria for Fried Frailty Phenotype

Table 1: Participant Characteristics by Modified Fried Frailty Phenotype

Characteristics	Overall (N=38,429)	Robust (N=25,347)	Prefrail (N=12,416)	Frail (N=666)	p
Age (years)	63.8±2.8	63.8±2.8	63.9±2.8	64.0±2.8	<0.01[b]
Sex					<0.01
Female	19,874 (52%)	12,528 (49%)	6,916 (56%)	430 (65%)	
Male	18,555 (48%)	12,819 (51%)	5,500 (44%)	236 (35%)	
Weight status (BMI)					<0.01
Normal weight	13,576 (35%)	9,986 (39%)	3,499 (28%)	91 (14%)	
Overweight	17,144 (45%)	11,605 (46%)	5,348 (43%)	191 (29%)	
Obese	7,539 (20%)	3,646 (14%)	3,516 (28%)	377 (57%)	
Race					<0.01
White	36,089 (94%)	23,946 (94%)	11,539 (93%)	604 (91%)	
Nonwhite	2,340 (6%)	1,401 (6%)	877 (7%)	62 (9%)	
Education qualification					<0.01
College	14,321 (37%)	10,022 (40%)	4,139 (33%)	160 (24%)	
Secondary	13,338 (35%)	8,691 (34%)	4,403 (35%)	244 (37%)	
Professional	5,137 (13%)	3,322 (13%)	1,735 (14%)	80 (12%)	
Smoke status					<0.01
Never	19,834 (52%)	13,381 (53%)	6,163 (50%)	290 (44%)	
Past	16,491 (43%)	10,701 (42%)	5,467 (44%)	323 (48%)	
Current	1,993 (5.2%)	1,199 (4.7%)	745 (6.0%)	49 (7.4%)	
Alcohol consumption					<0.01
Three	20,301 (53%)	14,381 (57%)	5,750 (46%)	170 (26%)	
One	15825 (41%)	9,722 (38%)	5,716 (46%)	387 (58%)	
Never	2,287 (6%)	1,236 (4.9%)	945 (7.6%)	106 (16%)	
Self-rated health status					<0.01
Good	31,636 (82%)	22,370 (88%)	9,083 (73%)	183 (27%)	
Fair	6,721 (17%)	2,944 (12%)	3,300 (27%)	477 (72%)	
Mean acceleration (mg)	25.7±7.2	26.5±7.1	24.6±7.1	20.0±5.9	<0.01
Time in MVPA (min/day)	62.0±32.6	65.6±32.4	56.1±31.7	35.3±23.3	<0.01

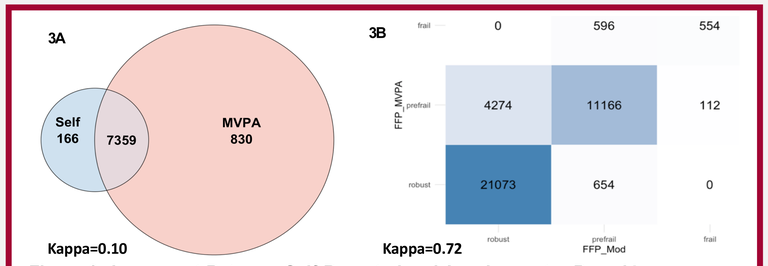
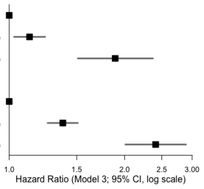


Figure 3. Agreement Between Self-Reported and Accelerometer-Based Low Physical Activity (3A) and Fried Frailty Phenotype (3B)

4A: All-cause mortality

FFP Definitions	Frailty Status	No. of Participants	No. of Deaths	Deaths per 10k PY	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
FFP-Mod							
	Robust	25,347	1,310	75.4	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]
	Prefrail	12,416	815	96.4	1.32 (1.21–1.44)	1.21 (1.10–1.32)	1.13 (1.03–1.24)
	Frail	666	100	229.4	3.37 (2.75–4.13)	2.38 (1.91–2.97)	1.89 (1.51–2.37)
FFP-MVPA							
	Robust	21,727	957	64.0	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]
	Prefrail	15,552	1,090	103.4	1.58 (1.45–1.72)	1.44 (1.32–1.58)	1.38 (1.26–1.51)
	Frail	1,150	178	237.3	3.76 (3.20–4.42)	2.89 (2.43–3.45)	2.41 (2.01–2.89)



4B: CVD mortality

FFP Definitions	Frailty Status	No. of Participants	No. of Deaths	Deaths per 10k PY	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
FFP-Mod							
	Robust	25,347	271	15.6	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]
	Prefrail	12,416	180	21.3	1.43 (1.19–1.73)	1.23 (1.01–1.50)	1.13 (0.93–1.38)
	Frail	666	20	45.9	3.42 (2.17–5.38)	2.11 (1.29–3.46)	1.57 (0.95–2.60)
FFP-MVPA							
	Robust	21,727	180	12.0	1.00 [Ref]	1.00 [Ref]	1.00 [Ref]
	Prefrail	15,552	250	23.7	1.92 (1.59–2.33)	1.67 (1.37–2.05)	1.57 (1.29–1.93)
	Frail	1,150	41	54.7	4.70 (3.34–6.61)	3.12 (2.14–4.54)	2.48 (1.68–3.66)

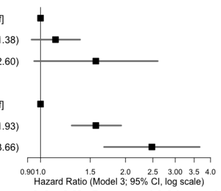


Figure 4. Associations of Fried Frailty Phenotype Definitions with All-Cause (4A) and Cardiovascular Disease (4B) Mortality

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; FFP-Mod, modified Fried Frailty Phenotype with questionnaire determined low physical activity; FFP-MVPA, Fried Frailty Phenotype with moderate-to-vigorous physical activity time determined low physical activity; HR, hazard ratio; PY, person-years; Ref, reference.

Model 1 adjusted for age and sex. Model 2 adjusted for Model 1 covariates + race, body mass index (BMI), education, smoking, alcohol intake, and diet. Model 3 adjusted for Model 2 covariates + self-rated health.

METHODS (CONT'D)

- **Mortality Ascertainment**:
  - Death records were obtained from the National Health Service Information Centre (England and Wales) and the National Health Service Central Register (Scotland).[4]
  - Participants were followed through November 2021.
- **Statistical Analyses**:
  - Agreement of FFP definitions was assessed using Cohen's kappa.
  - Cox models were used to examine and compare associations of FFP-MVPA and FFP-Mod with all-cause and CVD mortality.

RESULTS

- Over a median 6.95 years, 2,225 all-cause and 471 CVD deaths occurred. FFP-Mod and FFP-MVPA classified 666 and 1,150 participants as frail.
- Compared to robust individuals, frail individuals had 1.89 (1.51–2.37) times risk of all-cause mortality based on FFP-Mod and 2.41 (2.01–2.89) times risk based on FFP-MVPA. Pre-frail individuals had 1.13 (1.03–1.24) times risk based on FFP-Mod and 1.38 (1.26–1.51) based on FFP-MVPA, with non-overlapping CIs between these estimates (Figure 4A).
- Significant associations with CVD mortality were observed only for FFP-MVPA, with frail individuals having 2.48 (1.68–3.66) times risk and prefrail individuals having 1.57 (1.29–1.93) times risk; no significant associations were observed for FFP-Mod (Figure 4B).

CONCLUSIONS

- **Integrating accelerometer-derived PA into frailty assessment enhances the predictive validity of FFP for mortality.**
- **Accelerometer-based FFP definition demonstrated improved sensitivity in identifying prefrail individuals at risk of all-cause mortality and better ability to detect CVD mortality risk.**
- **Our findings highlight the clinical relevance of integrating accelerometer metrics into frailty assessments to facilitate earlier identification of health decline in older adults.**

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