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The influence of multiple frailty profiles on institutionalization and all-cause mortality in community-living older adults

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Abstract

Background Frailty in older adults is associated with adverse geriatric outcomes. Physical frailty is often accompanied by problems in the cognitive, psychological, and social domains. This study investigated the ability of physical frailty combined with other health domains to predict institutionalization and mortality.

Methods A national sample of 9171 Koreans aged 65 years or older were surveyed at baseline in 2008 and 3 year follow-up. Those who were prefrail or frail according to the Fried criteria were conceived to have physical frailty. Psychological frailty, cognitive frailty, and social frailty were defined as having depressive symptoms, cognitive impairment, and social vulnerabilities, respectively, in addition to physical frailty. Using Cox proportional hazards and competing-risks regression, the risk of mortality and institutionalization by the number and profiles of different frailty domains was analysed.

Results At baseline, the 9171 participants were aged 73.1 (±6.8) years on average (median: 72, range: 65 to 103), and 59.2% were women. Multidomain frailty was highly prevalent (49.3%), with 6.1% concurrently displaying frailty in all four domains (mixed frailty). The risk of negative health outcomes increased with frailty in a higher number of domains with a subhazard ratio (SHR) of 3.48 (95% confidence interval [CI]: 1.83, 6.62; $P < 0.001$) for institutionalization and a hazard ratio (HR) of 3.95 (95% CI: 2.62, 5.93; $P < 0.001$) for mortality among those presenting mixed frailty. Psychological frailty (depressive symptoms combined with physical frailty) was strongly predictive of institutionalization (SHR = 2.85; 95% CI: 1.45, 5.59; $P = 0.002$) and mortality (HR = 2.47; 95% CI: 1.61, 3.78; $P < 0.001$). When combined with physical frailty and either depressive symptoms or social vulnerabilities, cognitive impairment also exhibited a significantly elevated risk of negative events. Physical frailty alone was not a strong predictor of adverse events, especially for mortality (HR = 1.13; 95% CI: 0.77, 1.67; $P = 0.53$).

Conclusions Co-occurrence of physical frailty with other domains is common in late life. The presence of frailty in multiple domains raises the risk of adverse outcomes, with the effects varying by multidimensional profiles.

Keywords Frailty; Institutionalization; Mortality; Depression; Cognitive impairment; Social vulnerability

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Introduction

Frailty is a clinical syndrome of accelerated aging that causes a progressive loss of physiologic reserves, predisposing older people to increased vulnerability to stress and decreased resilience. It affects multiple systems, elevating the risk of adverse outcomes, such as disability, institutionalization, and mortality.[1]

Although initially defined as a physical construct, frailty is closely linked to other health dimensions, such as cognitive, psychological, and social functioning. Although impaired physical function is a hallmark of frailty, cognitive status and psychological well-being are also affected in frail or prefrail individuals.[2] In addition, physical frailty has been demonstrated to be strongly associated with cognitive impairment,[3] depression,[4] and social vulnerability.[5]

More recently, increasing attention has been directed towards conceptualizing frailty as a multidimensional construct.[6] Various definitions of cognitive frailty,[7] psychological frailty,[8] and social frailty[9] have been proposed. A multidimensional approach to frailty encompassing different domains is useful in predicting adverse outcomes, such as disability and mortality.[10,11] Cognitive frailty, defined as a combination of physical frailty and cognitive impairment, increased the risk of functional disability, low quality of life, and mortality.[12,13] The co-occurrence of frailty with depression[14] and social deficits[9] showed a significantly elevated mortality risk. Given that the core concept of frailty is grounded in its physical phenotype, it is important to determine whether different sets of cognitive, psychological, and social functioning domains influence or reinforce physical frailty in predicting adverse outcomes. A classification of physical frailty into distinct profiles according to different combinations of multiple domains would help to characterize and differentiate the impact of those domains.

The combined effects of different dimensions of frailty on adverse outcomes are poorly understood. Previous studies using multidimensional frailty scales have primarily focused on measuring the number of accumulated deficits, commonly deriving a summed score.[15] Moreover, the few studies examining the combined effects of multiple frailty domains have produced mixed results.[16–18] The extent to which different profiles of frailty influence adverse outcomes has not been rigorously evaluated.

This study explored patterns of different combinations or profiles of frailty and examined the predictive value of the accumulation of different functional domains on physical frailty on institutionalization and mortality in older adults living in the community.

Methods

Data source

The Living Profiles of Older People (LPOPS) is a national survey of community-dwelling adults aged 60 years and older (n = 19 007) in South Korea.[19] Details of the survey design have been provided elsewhere.[9] Briefly, a stratified two-stage cluster sampling design was used for which in-person interviews of 15 146 individuals were completed at baseline in 2008, with a response rate of 79.7%. Of the 12 087 participants aged 65 years and older, data for the 9171 persons were used in the final analysis after excluding missing data and those affected in domains other than physical frailty (Supporting Information, *Figure* S1). The Institutional Review Board at Keimyung University (IRB No. 08-52), the administrator of the project, approved the study's protocol. All study participants signed informed consent forms prior to taking part in the survey.

Measurements

To operationalize multiple profiles of frailty, physical frailty was considered the core construct, as it is a specific medical syndrome[20] and is known to be the strongest predictor of adverse health outcomes among the different dimensions of frailty.[17,21] Physical frailty was assessed according to the Fried phenotype model consisting of five criteria: shrinking (unintentional weight loss), weakness, poor endurance (exhaustion), slowness, and low activity.[1] The shrinkage criterion was met if the respondent reported losing 5 kg or more in the past 6 months. Exhaustion was operationalized using the two items on lack of energy and reduced endurance from the Center for Epidemiological Studies-Depression.[22] Low activity was determined by the total energy expended based on the International Physical Activity Questionnaire.[23] Slowness was identified based on the 2.5 m usual gait speed. Weakness was defined as the lowest quintile of grip strength using a Tanita hand dynamometer. Details of the frailty assessment have been reported elsewhere.[9] According to the number of components (out of a total of five) for which participants had values indicating frailty, the existence of 3 to 5 was defined as frail, 1 to 2 as prefrail, while having none was referred to as robust. In this study we defined physical frailty as being prefrail or frail.

Building on the foundation of physical frailty, other domains of functioning were combined to generate multiple frailty profiles. The two-domain profiles included cognitive frailty, psychological frailty, and social frailty. Cognitive frailty was defined as the presence of both cognitive impairment

and physical frailty. Individuals scoring more than 1.5 standard deviations below the age-specific, sex-specific, and education-specific norm on the Mini-Mental State Examination[24] were considered to have cognitive impairment. Psychological frailty was conceptualized as having depressive symptoms, defined as ≥8 on the short-form of the Geriatric Depression Scale[25] in addition to physical frailty. Social frailty was defined as the combination of physical frailty and having two or more among the nine social deficits (no formal education, not married, low income, living alone, no relatives/friends/neighbours, rarely having contact with relatives/friends/neighbours, not receiving social support, not providing social support, not participating in social activities).[9] The three-domain profiles included psycho-cognitive frailty, psychosocial frailty, and socio-cognitive frailty, accordingly. The presence of all four domains of frailty was termed mixed frailty. Those without physical frailty or other functional domains affected were considered to be robust.

The outcome variables were institutionalization and mortality. Institutionalization included admissions to hospitals or nursing homes during follow-up. Deaths were registered by interviewing the next of kin, often a spouse or child of the deceased, during a follow-up survey in 2011. The month and year of institutionalization or death were recorded for each person. The longest follow-up before censoring was 3.3 years.

The covariates considered were sociodemographic characteristics, health behaviours, and health conditions. Sociodemographic characteristics included age; sex; education (none, elementary school, middle/high school, and college or higher); marital status (married or not married [widowed, single, divorced, or separated]); income (household income divided by the square root of household size, in quartiles); and living alone. Health behaviours included smoking (never, former, or current smoking); alcohol consumption (abstinent, moderate [up to 7 drinks/week for women and 14 drinks/week for men], or heavy); and physical activity (recommended level defined as ≥75 min/week of vigorous-intensity or ≥150 min/week of moderate-intensity of aerobic activities). In addition, physician-diagnosed chronic diseases of hypertension, angina, stroke, type 2 diabetes, chronic bronchitis/emphysema, asthma, arthritis, fracture, chronic renal failure, and cancer were included, with the number of co-morbidities being categorized as 0, 1, and ≥2.

Statistical analysis

The number and profiles of multiple frailty domains by baseline characteristics were analysed using the chi-square test and analysis of variance. Kaplan–Meier survival curves were constructed to observe the probability of mortality during the follow-up period. A Cox proportional hazards model was used to analyse the mortality risk by the number of frailty types and multiple frailty profiles. For calculating the risk of institutionalization, a competing-risks model,[26] treating mortality as a competing risk, was used to derive cumulative incidence functions. Subdistribution hazard ratios were estimated, adjusting for age, sex, smoking, alcohol drinking, and co-morbidities as covariates. Variables, such as physical activity and socioeconomic status, comprising the multiple frailty profiles were not adjusted in the multivariable model. The absence of violation of the proportionality assumption was verified by log-minus-log survival plots and the Schoenfeld test ($P > 0.05$). The assumption of proportionality of subhazards was found to be met when a test was conducted for interaction between time and the number of frailty domains. A sensitivity analysis was performed where missing values on the predictor variables were imputed using the multiple imputations with chained equations methods. All statistical tests were two-sided, with a 0.05 significance level. Stata 16.1 (StataCorp, College Station, TX, USA) was used in all analyses, applying sampling weights to account for the complex survey design.

Results

Among the participants, 30.6% were robust, while 20.1% had only physical frailty. For those with multiple frailty domains, 25.2% had frailty in two domains, 18.0% in three domains, and 6.1% in all four domains (*Figure* S2). Social frailty was the most frequent two-domain profile (9.8%), while psychosocial frailty was the most common three-domain profile (10.0%).

At baseline, the respondents were aged 73.1 (±6.8) years on average (median: 72, range: 65 to 103), and 59.2% were women, 66.2% had received a formal education, 33.8% were not married, and 18.1% lived alone (*Table* 1). Participants with frailty in more domains tended to be older, women, less educated, not married, low-income, and living alone. They were also more likely to be non-smokers and non-drinkers and less likely to engage in physical activity. Frailty in a higher number of domains was associated with the presence of more co-morbidities.

Respondents with frailty in the social domain were more likely to be older, women, less educated, not married, lower-income, and living alone (*Table* 2). Those presenting only physical frailty were more likely to smoke or consume alcohol currently, while those having cognitive frailty or psycho-cognitive frailty demonstrated a higher likelihood of having a history of smoking. In the mixed frailty group, followed by the psychosocial or psychological frailty groups, few participants engaged in physical activity. Those with frailty in the psychological domain also tended to exhibit higher rates of co-morbidities.

Kaplan–Meier survival curves for mortality revealed a significant difference in the survival probability for mortality (log-rank test, $\chi^2_{(4)} = 179.52$, $P < 0.001$), demonstrating a

Table 1 Baseline sample characteristics by number of frailty domains (n = 9171)

	Total	Number of frailty domains				
		0	1	2	3	4
Age, year	73.1 ± 6.8	70.3 ± 4.8	72.3 ± 6.1	74.2 ± 7.0	75.4 ± 7.4	78.0 ± 8.9
Women	59.2	48.6	53.5	66.7	69.8	68.4
Education						
None	33.8	14.3	25.8	43.8	53.5	59.0
Elementary school	37.4	42.5	42.3	36.2	28.2	27.7
Middle/high school	21.5	28.8	23.4	17.1	16.3	12.0
≥College	7.3	14.4	8.5	3.0	2.0	1.3
Not married	33.8	15.3	21.5	41.4	56.7	68.8
Income (Q_1)[a]	25.6	11.4	14.8	31.6	44.7	52.0
Living alone	18.1	5.7	5.5	23.9	37.8	39.3
Smoking						
Never	65.8	61.0	66.2	69.6	67.5	67.3
Former	20.6	24.4	19.2	17.6	20.0	20.3
Current	13.6	14.6	14.6	12.8	12.5	12.4
Alcohol drinking[b]						
None	68.0	59.1	64.5	72.0	77.4	80.9
Moderate	23.3	29.9	25.9	20.6	16.5	12.8
Heavy	8.7	11.0	9.6	7.4	6.1	6.3
Physical activity[c]	16.9	31.0	16.2	11.5	6.0	3.6
Co-morbidities[d]						
0	26.6	37.4	28.0	21.8	17.2	16.4
1	36.6	37.0	38.1	36.6	34.0	37.0
≥2	36.8	25.6	33.9	41.6	48.8	46.6

Values denote percentages or mean ± standard deviation. The chi-square test and analysis of variance yielded significant results ($P < 0.01$) in all cases.
[a]Equivalent income (household income divided by the square root of household size) in the lowest quartile.
[b]Moderate: up to 7 drinks/week for women and 14 drinks/week for men.
[c]Recommended aerobic physical activity (≥ 75 min/week of vigorous-intensity or ≥ 150 min/week of moderate-intensity).
[d]Number of co-morbid conditions (hypertension, stroke, angina, diabetes mellitus, arthritis, chronic bronchitis/emphysema, asthma, cancer, chronic renal failure, fracture).

trend ($P < 0.001$) of increasing risk with frailty in a higher number of domains (*Figure* 1). In addition, there was a positive association between the number of domains of frailty and the cumulative incidence of institutionalization, exhibiting a widening difference over time between the multiple frailty groups and the single (physical only) frailty group.

The risk of adverse outcomes increased with the presence of frailty in a higher number of domains (*Table* 3). Physical frailty alone was significantly predictive of institutionalization but not mortality, whereas the presentation of two or more frailty domains was significantly associated with increased hazards for both outcomes. In the adjusted analysis, compared with the robust group, the mixed frailty group, in whom all four domains were affected, demonstrated a 3.5-fold and 4-fold increase in the risk of institutionalization and death, respectively.

The risk of adverse outcomes varied by different frailty profiles (*Table* 4). Among the two-frailty profiles, psychological frailty was significantly associated with institutionalization (subhazard ratio [SHR] = 3.83, 95% CI: 1.97, 7.44) and mortality (hazard ratio [HR] = 3.01, 95% CI: 2.02, 4.49), even after adjusting for covariates. Social frailty was significantly predictive of the two negative outcomes in the unadjusted analysis, but the association became nonsignificant when adjusted for covariates. However, socially frail participants with either depressive symptoms or cognitive impairment were significantly at risk of adverse events. Cognitive frailty was significant for predicting mortality, but not institutionalization; however, when it was combined with the psychological domain (psycho-cognitive frailty) or social domain (socio-cognitive frailty), there was a 3.2-fold and 3.9-fold increased risk, respectively. Those with mixed frailty displayed the highest risk of mortality.

Sensitivity analyses using multiple imputations did not significantly alter the results (*Tables* S1 and S2). Minor exceptions were noted. For those with physical frailty alone, the risk for institutionalization was slightly reduced (P = 0.050). The strength of the association between cognitive frailty and mortality was also diminished to borderline significance (P = 0.060).

Discussion

In community-dwelling older adults, the presence of frailty in multiple domains (cognitive, psychological, and social) in addition to physical frailty was predictive of institutionalization and mortality in patterns specific to particular multidomain profiles. Multidimensional frailty was prevalent, with about a half of older participants exhibiting frailty in two or more functional domains. The presence of frailty in multiple do-

Table 2 Baseline sample characteristics by multiple frailty profiles (n = 9171)

		Number of frailty domains/frailty profiles								
		0	1	2			3			4
	Total	Robust	Phys	Cog	Psy	Soc	PsyCog	PsySoc	SocCog	Mixed
Age, year	73.1 ± 6.8	70.3 ± 4.9	72.3 ± 6.1	72.4 ± 6.0	72.9 ± 6.1	76.5 ± 7.8	72.8 ± 6.0	76.0 ± 7.2	78.1 ± 8.7	78.0 ± 8.9
Women	59.2	48.6	53.5	44.6	65.4	82.9	42.0	85.2	68.5	68.4
Education										
None	33.8	14.3	25.8	8.7	37.6	73.2	15.8	75.4	48.1	59.0
Elementary school	37.4	42.5	42.3	50.7	43.7	19.6	45.6	18.6	28.7	27.7
Middle/high school	21.5	28.8	23.4	34.4	15.8	6.4	33.1	5.4	23.2	12.0
≥College	7.3	14.4	8.5	6.2	2.9	0.8	5.5	0.6	0.0	1.3
Not married	33.8	15.3	21.5	15.6	22.0	76.2	12.7	78.3	65.7	68.8
Income (Q_1)[a]	25.6	11.4	14.8	14.9	22.8	50.8	16.5	58.5	50.5	52.0
Living alone	18.1	5.7	5.5	4.2	3.9	55.1	3.2	56.9	36.5	39.3
Smoking										
Never	65.8	61.0	66.2	60.4	65.9	79.2	51.1	74.0	76.8	67.3
Former	20.6	24.4	19.2	25.8	19.6	10.3	35.1	13.2	14.6	20.3
Current	13.6	14.6	14.6	13.8	14.5	10.5	13.8	12.8	8.6	12.4
Alcohol drinking[b]										
None	68.0	59.1	64.5	62.3	74.9	76.0	72.8	78.5	82.5	80.9
Moderate	23.3	29.9	25.9	25.8	18.8	18.7	20.2	15.8	12.0	12.8
Heavy	8.7	11.0	9.6	11.9	6.3	5.3	7.1	5.7	5.5	6.3
Physical activity[c]	16.9	31.0	16.2	20.0	7.7	9.0	9.0	4.3	6.2	3.6
Co-morbidities[d]										
0	26.6	37.4	28.0	23.5	16.8	24.9	16.0	15.0	28.1	16.4
1	36.6	36.9	38.1	39.4	36.2	35.2	32.9	33.5	38.0	37.0
≥2	36.8	25.6	33.9	37.1	47.0	39.9	51.1	51.5	33.9	46.6

Phys, physical frailty only; Cog, cognitive frailty; Psy, psychological frailty; Soc, social frailty; PsyCog, psycho-cognitive frailty; PsySoc, psychosocial frailty; SocCog, socio-cognitive frailty; Mixed, psychosocio-cognitive frailty.
Values denote percentages or mean ± standard deviation. The χ^2 test and analysis of variance yielded significant results ($P < 0.01$) in all cases.
[a]Equivalent income (household income divided by the square root of household size), in the lowest quartile.
[b]Moderate: up to 7 drinks/week for women and 14 drinks/week for men.
[c]Recommended aerobic physical activity (≥75 min/week of vigorous-intensity or ≥150 min/week of moderate-intensity).
[d]Number of co-morbid conditions (hypertension, stroke, angina, diabetes mellitus, arthritis, chronic bronchitis/emphysema, asthma, cancer, chronic renal failure, and fracture).

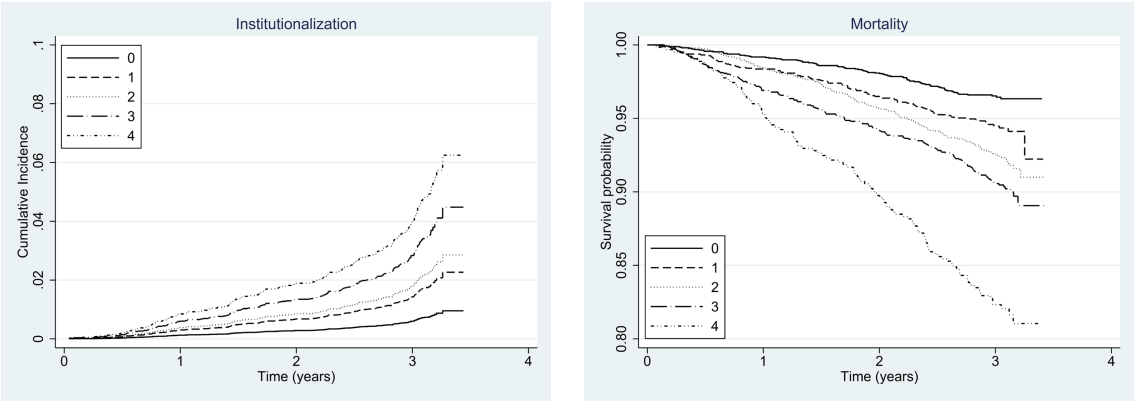

Figure 1 Cumulative incidence curves for institutionalization (left) and Kaplan–Meier survival curves for mortality (right) according to the baseline number of frailty domains.

mains reinforced the effect of physical frailty on adverse outcomes.

Our finding that frailty in multiple domains had predictive power is consistent with the results from two prior studies. First, a study of rural residents aged 75 years or older in Spain reported 3 year mortality hazard ratios of 1.9, 3.9, and 10.4 for participants with 1, 2, and 3 domains of frailty (physical, mental, and social), respectively.[18] Simi-

Table 3 Risk of institutionalization and mortality by number of frailty domains (n = 9171)

	Institutionalization, SHR (95% CI)	Mortality, HR (95% CI)
Unadjusted model		
0	1.00	1.00
1	2.39 (1.29, 4.44)	1.35 (0.92, 1.96)
2	3.02 (1.72, 5.33)	2.28 (1.67, 3.12)
3	4.79 (2.75, 8.33)	2.63 (1.89, 3.66)
4	6.74 (3.66, 12.41)	6.87 (4.77, 9.89)
Adjusted model[a]		
0	1.00	1.00
1	1.97 (1.05, 3.67)	1.14 (0.77, 1.67)
2	2.07 (1.16, 3.67)	1.81 (1.29, 2.54)
3	2.89 (1.63, 5.12)	1.91 (1.33, 2.73)
4	3.48 (1.83, 6.62)	3.95 (2.62, 5.93)

SHR, subhazard ratio; HR, hazard ratio; CI, confidence interval.
[a]Adjusted for age, sex, smoking, alcohol drinking, and co-morbidities.

larly, among community-dwelling Singaporean Chinese aged 55 years or older, the addition of mental and social frailty to physical frailty contributed to more than a two-fold increase in the risk of disability, nursing home referral, and mortality at 2 year follow-up.[17] In contrast, in a sample of community-living, physically frail residents aged 70 years or older in the southern part of the Netherlands, cognitive, psychological, and social frailty dimensions were not predictive of disability or hospitalizations at 1 year.[16] The Dutch study, however, did not evaluate the combined effects of different frailty domains.

Prior studies are limited in that they did not analyse in detail the effects of the co-occurrence of multiple domains of frailty. In this study, multiple frailty profiles were identified and found to predict adverse outcomes differentially. Among the two domain profiles, psychological frailty (a combination of physical frailty with depressive symptoms) was the strongest predictor of institutionalization and mortality. Depression is a well-known predictor of poor health outcomes, such as nursing home admission[27] and mortality.[28] The coexistence of depression and frailty is common in older people and has been reported to increase mortality risk.[14,29] Depression also substantially explained variation in nursing home placement to a similar degree as frailty.[30] Depression and frailty have overlapping constructs, shared symptomatology, risk factors, and outcomes, exhibiting reciprocal relationships.[4] Depression may exacerbate physical frailty as it represents a lack of psychological and social resources to cope with stressors.[31]

In contrast, cognitive frailty or social frailty was not found to be a very strong predictor of adverse outcomes. Although cognitive frailty by itself did not significantly increase the risk, when combined with depressive symptoms (psycho-cognitive frailty) or social vulnerabilities (socio-cognitive frailty) the risk of both institutionalizations and deaths noticeably increased. Alternatively, physically frail individuals with social deficits demonstrated a higher risk of institutionalization and mortality only when they also had depressive symptoms (psychosocial frailty) or cognitive impairment (socio-cognitive frailty). Depression, cognitive impairment, and frailty are closely related to one another. Depressive symptoms and cognitive impairment often co-occur in late life, with cognitive deficits persisting even after the remission of depression.[32] Further, the presence of physical frailty in late-life depression appears to worsen cognitive performance,[33] which might contribute to deleterious health effects. In a study that classified late-life depression into different subtypes, those manifesting a combined depressive and cognitive symptomatology with physical frailty had the lowest remission rate and highest mortality.[34] Additionally, social deprivation—in particular less education and infrequent social contacts, which are known risk factors of cognitive decline and dementia[35]—might negatively affect cognitive ability in frail older people, raising the probability of adverse outcomes. Social vulnerability, characterized as a lack of socioeconomic resources and low social support and participation, coupled with frailty, has been found to confer high mortality risk in older adults.[9,36] In the Honolulu-Asian Aging Study,[37] the accumulation of social vulnerabilities and frailty was strongly associated with both cognitive decline and mortality. Socially deprived older adults may lack resources to receive care in their homes,[38] and are therefore more likely to be institutionalized when they become frail or cognitively impaired. Frail older pa-

Table 4 Risk of institutionalization and mortality by multiple frailty profiles (n = 9171)

Number of frailty domains	Frailty profiles	Institutionalization, SHR (95% CI)		Mortality, HR (95% CI)	
		Unadjusted model	Adjusted model[a]	Unadjusted model	Adjusted model[a]
0	Robust	1.00	1.00	1.00	1.00
1	Physical frailty only	2.39 (1.29, 4.44)	1.96 (1.05, 3.65)	1.35 (0.92, 1.96)	1.13 (0.77, 1.67)
2	Cognitive frailty	2.25 (0.99, 5.08)	1.92 (0.84, 4.37)	1.98 (1.30, 3.02)	1.53 (1.01, 2.34)
	Psychological frailty	3.83 (1.97, 7.44)	2.85 (1.45, 5.59)	3.01 (2.02, 4.49)	2.47 (1.61, 3.78)
	Social frailty	2.90 (1.50, 5.60)	1.64 (0.84, 3.20)	1.86 (1.29, 2.69)	1.42 (0.96, 2.10)
3	Psycho-cognitive frailty	4.02 (1.94, 8.34)	3.18 (1.52, 6.64)	2.95 (1.90, 4.58)	1.97 (1.26, 3.10)
	Psychosocial frailty	4.44 (2.44, 8.09)	2.45 (1.32, 4.54)	2.07 (1.43, 3.00)	1.65 (1.10, 2.48)
	Socio-cognitive frailty	7.79 (3.74, 16.26)	3.94 (1.80, 8.62)	4.16 (2.48, 6.99)	2.41 (1.40, 4.15)
4	Mixed frailty	6.74 (3.66, 12.42)	3.42 (1.79, 6.52)	6.87 (4.77, 9.89)	3.89 (2.57, 5.85)

SHR, subhazard ratio; HR, hazard ratio; CI, confidence interval.
[a]Adjusted for age, sex, smoking, alcohol drinking, and co-morbidities.

tients with low psychosocial resources such as poor well-being, low sense of control, and low social activities were reported to have an elevated risk of higher level-of-care transitions and mortality.[39]

It is noteworthy that being affected in only the physical domain of frailty was not a strong predictor of adverse outcomes, especially for mortality. This appears to run counter to consistent reports of frailty predicting hospitalizations, nursing home admissions, and mortality.[40] However, previous studies have not explicitly identified those who exhibit only the physical domain of frailty. Studies based on a phenotypic model tend to group people with physical frailty alone and those with physical frailty mixed with other domains as a single entity. Research using the frailty index based on the accumulated deficit model has not usually delineated the independent role of physical frailty. It may be that those solely affected by the physical dimension of frailty are in an early stage of its progression, too far from death for physical frailty itself to be a predictive factor. This is partially supported by the finding that the physical frailty profile presented the lowest mean number of Fried's phenotypes (*Table* S3). Furthermore, the physical frailty profile showed higher cognitive, psychological, and social functioning levels compared with other frailty profiles. Over time, the accumulation of deficits across multiple domains of frailty in conjunction with the deterioration in physical frailty may predispose older people to a greater mortality risk. Defining the physical domain of frailty as $\geq$3 Fried phenotypes did not significantly alter the results, with the small cell sizes likely resulting in sparse data bias (data not shown).

The influence of other domains of functioning (cognitive, psychological, social) besides physical frailty on adverse outcomes was not as strong (*Table* S4). Among those with only one of the domains affected, only the cognitively impaired showed a significant relationship with mortality, though in the opposite direction. With the concurrence of two or three of the domains, however, more significant associations emerged. Among the two-domain profiles, those who were depressed and socially vulnerable were at an increased risk for institutionalization and mortality. The cognitively impaired, having either depressive symptoms or social deficits, showed a reduced risk for institutionalization, though the sample size was too small to give credence to the precision of the estimates. Those with all three of the cognitive, psychological, and social domains affected presented with a significantly elevated risk for mortality but not for institutionalization. In contrast, physical frailty combined with other domains consistently predicted adverse outcomes, supporting the notion of the physical domain as the central construct in conceptualizing multiple frailty profiles as a prognostic indicator.

A major strength of this study is that the study population came from a nationally representative sample of community-dwelling older adults, giving credence to the generalizability of the findings. Sensitivity analyses with multiple imputations produced similar results, supporting the robustness of the results. Multiple domains of frailty were considered in the aggregate and by different combinations. The construction of multiple frailty profiles had the added benefit of incorporating both the unidimensional phenotype model and the multidimensional accumulation of deficits model of the frailty concept.

Several study limitations, however, need some consideration. One is the inherent limitation of the longitudinal design, where differential attrition might have diminished the study's external validity. However, compared with participants, those lost to follow-up tended to be slightly older but did not differ in other characteristics (*Table* S5). Second, in defining institutionalization, hospitalizations and nursing home admissions were grouped due to the small number of cases. Frailty in a higher number of domains tended to be associated with an increased risk of admission to a nursing home than to a hospital (data not shown). Third, the relatively short duration of follow-up prevented observing the effects of long-term changes in or trajectories of frailty states across different domains, which warrants future research.

In conclusion, this study revealed multidimensional frailty to be prevalent in older people living in the community. Operationalized as an accumulation of frailty and as distinct profiles, multiple domains of frailty were predictive of adverse outcomes. Given that frailty, construed solely as a physical construct, might have limited prognostic power for mortality, a better understanding of the combined effects of and interactions between different frailty domains would be instrumental in improving its prognostication and management.

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Conflict of interest

Yunhwan Lee, Eunsaem Kim, Jihye Yun, and Kumban Walter Chuck declare that they have no conflict of interest.

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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