Frailty Among Community-Dwelling Elderly People in France: The Three-City Study

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Background. To better understand the contribution of frailty to health-related outcomes in elderly persons, it seems valuable to explore data from cohort studies across the world in an attempt to establish a comprehensive definition. The purpose of this report is to show the characteristics of frailty and observe its prognosis in a large sample of French community-dwelling elderly persons.

Methods. We used data from 6078 persons 65 years old or older participating in the Three-City Study (3C). Frailty was defined as having at least three of the following criteria: weight loss, weakness, exhaustion, slowness, and low activity. Principal outcomes were incident disability, hospitalization, and death. Multiple covariates were used to test the predictive validity of frailty on these outcomes.

Results. Four hundred twenty-six individuals (7%) met frailty criteria. Participants classified as frail were significantly older, more likely to be female, and less educated and reported more chronic diseases, lower income, and poorer self-reported health status in comparison to nonfrail participants. In multivariate analysis, frailty was significantly associated with 4-year incidence of disability in activities of daily living (ADL) and instrumental ADL. However, frailty was marginally associated with incident hospitalization and was not a statistically significant predictor of incident mobility disability or mortality adjusting for potential confounding factors.

Conclusions. Frailty is not specific to a subgroup or region of the world. The construct proposed by Fried and colleagues confirms its predictive validity for adverse-health outcomes, particularly for certain components of disability, thus suggesting that it may be useful in population screening and predicting service needs.

Key Words: Frailty—Community-dwelling—Validity—Prognosis—Elderly.

FRAILTY has emerged as a condition associated with an increased risk of functional decline among the elderly population, which may be differentiated from aging, disability, and comorbidity (1). Frailty describes a state of vulnerability to the adverse effects of a variety of environmental stressors, expressed as an increased risk of accumulating health-related problems, hospitalization, need for long-term care, and death (2–6).

To identify frail individuals, several criteria have been proposed in recent years (3,7–10). According to the criteria used, heterogeneous results regarding frequency have been obtained when applied in clinical practice (11,12). Nevertheless, there is a general agreement that the core feature of frailty is increased vulnerability due to impairments in multiple, inter-related systems resulting in homeostatic reserve disturbance (3,13–16). Multiple impairments are demonstrated by the presence of a combination of several clinical characteristics, and it seems unlikely that a single altered system is sufficient to explain this clinical state (1,17). Recently, a working group proposed a definition that conceptualizes frailty as a clinical syndrome defined as the combination of shrinking, weakness, exhaustion, low walking speed, and low physical activity (3). This conception of frailty implies a biological connection between all its components and is widely used.

To better understand the role of frailty in health outcomes for different subgroups, it is important to examine data from cohort studies across cultures to assess its ability to predict adverse outcomes in different populations. Therefore, the purpose of this report is to describe the characteristics and prognosis of persons classified as "frail" in a large sample of French community-dwelling elderly persons. The main hypothesis is that frail persons defined according to the criteria derived from the study by Fried and colleagues present more adverse outcomes such as the incidence of disability, more frequent hospitalization, and mortality, even after adjustment for potential confounders.

METHODS

Study Population

The participants in the present study are a subset of the Three-City Study (3C), a multicenter study aiming to evaluate the risk of dementia and cognitive impairment attributable to vascular factors. The methodology has been previously reported (18). Briefly, it is a 4-year cohort study of 3650 men and 5644 women 65 years old or older, initially noninstitutionalized. The sample was drawn from a random sample obtained from the electoral rolls of three French cities—Bordeaux (southwest), Dijon (central east), and Montpellier (southeast)—between 1999 and 2000. Two follow-ups have been carried out (2001–2002 and 2003–2004). A wide range of information was collected during face-to-face interviews (using a standardized questionnaire) by trained nurses and psychologists, including sociodemographic characteristics, educational level, and lifestyle (smoking, alcohol use, and food intake). The examination included blood pressure, cognitive evaluation, and biological parameters. In addition, self-report of chronic diseases, depressive symptoms, and functional status were recorded. The 3C Study was approved by the Ethical Committee of the University Hospital of Kremlin-Bicêtre, and all participants provided written informed consent.

Definition of Frailty

Frailty was defined according to the construct previously validated by Fried and colleagues in the Cardiovascular Health Study (3). All five components from the original phenotype were retained for this study; however, the metrics used to characterize the frailty criteria were slightly different and defined as follows:

Shrinking.—Recent and unintentional weight loss of ≥ 3 kg was identified and body mass index calculated. Participants who answered ''yes'' for weight loss or had a body mass index < 21 kg/m^2 were considered to be frail for this component. This threshold is used in the Mini-Nutritional Assessment (19) and has been shown to be associated with increased mortality (20). In addition, it was previously associated with adverse outcomes in community-dwelling elderly persons in France (20,21).

Poor endurance and energy.—As indicated by self-report of exhaustion, identified by two questions from the Center for Epidemiological Studies-Depression scale [CES-D (22)]: ''I felt that everything I did was an effort'' and ''I could not get going.'' Participants were asked: ''How often, in the last week, did you feel this way?'' 0 = rarely or none of the time; 1 = some or a little of the time; 2 = a moderate amount of the time; or 3 = most of the time. Participants answering ''2'' or ''3'' to either of these questions were considered as frail by exhaustion.

Slowness.—The slowest quintile of the population was defined at baseline, based on a timed 6-meter walking test, adjusting for gender and height as recommended. The lowest quintile was used to identify participants with slowed walking speed.

Weakness.—Participants answering ''yes'' to the following question were categorized as frail for this component: ''Do you have difficulty rising from a chair?'' Grip strength, which evaluates the muscular power and force that can be generated with the hands, was not available in the 3C Study data set. However, a multidisciplinary expert consensus (nutritionist, neurologist, psychologist, and geriatrician) determined that the question was an adequate ''proxy'' for weakness. In addition, it was shown that grip strength significantly correlates with muscular power in other muscle groups among elderly persons [elbow flexion, knee extension, trunk extension, and trunk flexion (23)].

Low physical activity.—A single response was used to estimate physical activity (24). Individuals who denied doing daily leisure activities such as walking or gardening and/or denied doing some sport activity per week were categorized as physically inactive. Those who reported doing them were considered to be physically active.

As proposed by Fried and colleagues, the participants were considered to be ''frail'' if they had three or more frailty components among the five criteria; they were considered ''prefrail'' or ''intermediate'' if they fulfilled one or two frailty criteria, and ''nonfrail'' if none (3).

Outcomes

Three measurements of disability were investigated as outcomes: mobility, instrumental activities of daily living (IADL), and basic activities of daily living (ADL). Mobility was assessed by the Guttman's health scale (25): doing heavy housework, walking a half mile, and going up the stairs. For the IADL, participants reported their ability to perform eight IADLs based on the Lawton and Brody scale: using the telephone, having responsibility for one's own medication, managing money, being able to transport oneself, shopping, grooming, doing housework, and doing laundry [the last three were only asked of women (26)]. For the ADL, participants were asked if they needed help for any task from the Katz ADL scale [bathing, dressing, transferring from bed to chair, toileting, and feeding (27)]. For each domain of disability, if participants indicated that they were unable to perform one or more activities without help, they were considered as having mobility, IADL, or ADL disability (25–27). The 4-year incidence of disability was established only among participants without prevalent disability in the same domain at baseline.

Four-year incident hospitalization was considered when the participants declared it either at the first follow-up (2 years) or subsequent follow-up interview (4 years). Cause and time of death were obtained from interviews with family or from medical records at both follow-ups, and treated as cumulative 4-year mortality.

Covariates

Sociodemographic variables included age, sex, marital status, educational level, living alone, and monthly income. Participants were asked whether they had a physician's diagnosis of cardiac failure, myocardial infarction, angina pectoris, chronic obstructive pulmonary disease, fractures during the two preceding years (femoral or vertebral),

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┌─────────────────────────┐
│ Bordeaux and Dijon cities│
│       n = 7188           │
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┌──────────────────────────────────────────────┐
│ Eliminated from sample at baseline             │
│                                                │
│ n = 118    Parkinson's disease                 │
│ n = 45     Confined to bed                     │
│ n = 18     Blindness                           │
│ n = 29     Deafness                            │
│ n = 198    Demented                            │
│ n = 235    Previous stroke                     │
│ n = 467    Missing frailty score values        │
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┌─────────────────┐
│  Total sample   │
│    n = 6078     │
└─────────────────┘
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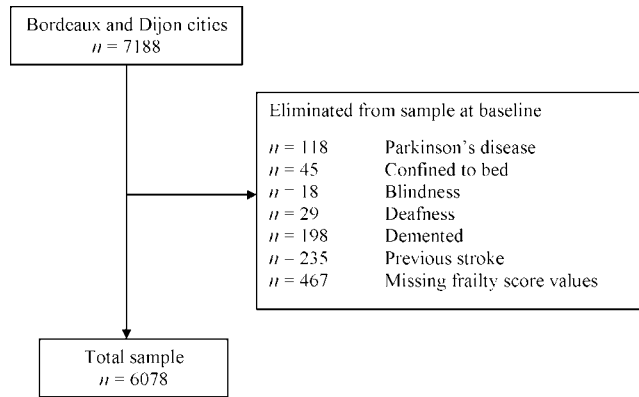
Figure 1. Assembly of the study sample selected among the Three-City Study.

cancer diagnosis, or arthrosis. Participants were considered as hypertensive if self-reported or systolic blood pressure was ≥ 160 mmHg or diastolic blood pressure was ≥ 95 mmHg or if they were on antihypertensive medications. Participants were considered as diabetics if self-reported or having high glucose level (≥ 7.0 mmol/L) or they were on hypoglycemic treatment (oral diabetic medications or insulin). The presence of each of these diseases was summed up in a score ranging from 0 to 9, where a higher score indicates more chronic disease. Self-reported health was also recorded and treated as a categorical variable (good, regular, or poor).

Depressive symptoms were assessed using the CES-D [20-item version (22,28)]. For the multivariate analyses, the two questions used for the frailty definition were excluded from the total CES-D score. Depressive symptoms were used as a continuous variable, and a higher score represents a worse mood.

The Mini-Mental State Examination [MMSE (29)] was used to assess global cognitive function (0–30 points; higher score indicates better cognitive status).

Smoking status (nonsmoker, former smoker, or current smoker) and usual alcohol intake (nondrinker, former drinker, or current drinker) were self-reported.

Plasma cholesterol total levels were used as continuous variable.

Sample

For the present research, only participants from two cities were considered, because in Montpellier, the timed walking test was not administered. Moreover, of the 7188 participants interviewed at baseline in Bordeaux and Dijon, those with conditions that could be a consequence of a single disease and not of generalized frailty as already proposed were excluded (3). In contrast, participants whose frailty status could not be determined (missing data) were also excluded (Figure 1). As expected, those excluded were significantly older (78.4 vs 74.1 years), more depressed (mean CES-D score 13.1 vs 8.1), and more likely to be disabled for mobility (80.6% vs 44.9%), IADL (29.3% vs 8.1%), and ADL (1.8% vs 0.4%). Data for 2354 (38.7%)

men and 3724 (61.3%) women, who had complete clinical and functional data at baseline, were finally included in the statistical analyses. Four-year incidence outcomes were computed as the sum of information concerning to the 2- and 4-year follow-ups.

Statistical Analysis

Variables were described using arithmetic means and standard deviations or frequencies and proportions where appropriate. The following statistical procedures were used according to the characteristics of each variable: chi-square test for qualitative data or analysis of variance for continuous data. Post hoc comparisons among the three frailty subgroups were conducted for continuous variables where indicated (Bonferroni correction). To determine the predictive validity of frailty definition in this cohort study, separate logistic regression models were used to describe the unadjusted effect of frailty on the 4-year incidence of mobility, IADL and ADL disability, and hospitalization. In a second model, multivariate logistic regression analyses were used to study the effect of frailty adjusting for covariates (3,30–32): age, sex, education level, income, smoking status, alcohol use, number of chronic diseases, self-reported health, CES-D score, and MMSE score. Incidence of IADL disability was also adjusted for baseline mobility disability, whereas for the analyses of incident ADL disability, baseline mobility and IADL disability were included. Baseline disability (mobility, IADL, and ADL) was also taken into account in the model related to the incidence of hospitalization. Additional adjustment for cholesterol levels had negligible impact, hence was not included. Contrary to disability and hospitalization (for which data were obtained only at the time of the follow-ups), for mortality date of death was available and allowed us to determine hazard ratios. A Cox proportional hazards model with delayed entry, in which the time-scale was the individual's age, was performed to estimate the cumulative risk of death and later was also performed using all variables mentioned above (except age), including baseline functional status, with frailty status as the main explanatory variable. All statistical tests were performed at the 0.05 level, and 95% confidence intervals were given. Statistical tests were performed using SPSS for Windows (version 13.0; SPSS Inc., Chicago, IL).

RESULTS

The study sample comprised 6078 individuals. Mean age was 74.1 years (range 65–95 years), and 61.3% were women (Table 1). Hypertension (64%), arthrosis (14.9%), chronic obstructive pulmonary disease (13.4%), and diabetes (9.3%) were the most frequent chronic diseases, and 29.9% of participants reported 2 or more of the chronic diseases. Forty-five percent had disability for mobility, 8.1% for IADL, and only 0.4% for ADL at baseline. Disability was higher in women than in men for mobility (52.0% vs 34.8%, respectively; $p < .001$) and IADL (9.6% vs 5.9%, respectively; $p < .001$), but for ADL the difference was not significant (0.3% vs 0.4%, respectively; $p = .166$). However, at older ages (≥ 85 years), the differences between the sexes were statistically significant for the three domains of

Table 1. Sociodemographic Characteristics and Health Status of Participants With Frailty at Baseline (The Three-City Study)

Variable	All N = 6078	Nonfrail N = 2756	Prefrail N = 2896	Frail N = 426	p
Age, mean (SD)	74.1 (5.2)	73.5 (5.1)[a]	74.4 (5.2)[b]	76.6 (5.5) [c]	<.001
Female gender (%)	61.3	57.0	63.5	77.2	<.001
High education level (%) (>12 y)	17.0	17.8	17.0	12.0	.029
Lives alone (%)	37.4	35.7	37.7	47.6	<.001
Monthly income <780 (%)	5.4	4.7	5.7	11.6	<.001
Poor self-reported health (%)	4.4	1.1	5.0	21.6	<.001
Hypertension (%)	64.0	63.9	63.1	70.9	.007
Diabetes (%)	9.3	8.9	10.1	14.7	.008
Cardiac failure (%)	5.7	3.9	6.5	11.5	<.001
Myocardial infarction (%)	4.6	3.9	5.0	6.9	.009
Angina pectoris (%)	8.5	6.2	9.4	16.8	<.001
Chronic obstructive pulmonary disease (%)	13.4	12.1	13.7	17.2	.221
Fractures (%)	6.4	5.5	6.9	8.8	.010
Cancer (%)	5.3	5.0	5.5	6.6	.350
Arthrosis (%)	14.9	11.0	17.2	26.4	<.001
Chronic diseases, mean (SD)	1.2 (1.0)	1.1 (0.9)	1.3 (1.0)	1.6 (1.1)	<.001
Current smoker (%)	5.5	4.8	6.3	4.2	<.001
Current drinker (%)	79.2	81.4	79.3	65.7	<.001
MMSE score, mean (SD)	27.4 (1.9)	27.5 (1.9)[a]	27.4 (1.9)[b]	26.9 (2.0)[c]	<.001
CES-D score, mean (SD)	8.1 (7.4)	5.6 (5.21)[a]	9.3 (7.84)[b]	15.7 (9.30)[c]	<.001
Cholesterol, mmol/L, mean (SD)	5.81 (1.0)	5.79 (0.9)	5.82 (1.0)	5.85 (1.1)	.356
Disability for mobility (%)	44.9	34.9	50.0	81.9	<.001
Disability ≥ 1 IADL task (%)	8.1	4.3	8.3	32.8	<.001
Disability ≥ 1 ADL task (%)	0.4	0.2	0.2	3.3	<.001

Notes: Chronic diseases: hypertension, diabetes, cardiac failure, myocardial infarction, angina pectoris, chronic obstructive pulmonary disease, fractures (femoral or vertebral), cancer, and arthrosis.

[a,b,c] Different letters indicate a statistically significant inter-group difference (Bonferroni's correction). *p* value represents the global test.

MMSE = Mini-Mental State Examination (0–30 points; higher score indicates better cognitive status); CES-D = Center for Epidemiological Studies-Depression scale (excluding the two questions used for the frailty definition; higher score indicates worse mood status; IADL = instrumental activities of daily living (self-reported disability); ADL = basic activities of daily living (self-reported disability).

disability ($p < .001$). Fifty-four percent of participants reported to be completely autonomous for the three domains of disability evaluated.

Table 2 presents the percentage for each component of frailty. Frailty was present in 426 (7.0%) individuals. Baseline comparison of demographic and health characteristics according to frailty status are shown in Table 1. As expected, participants classified as frail were older ($p < .001$), more likely to be female ($p < .001$), and less educated ($p = .029$), and they reported more chronic diseases ($p < .001$), lower income ($p < .001$), and poorer self-reported health status ($p < .001$) in comparison to prefrail or nonfrail participants. This subgroup also reported smoking and alcohol consumption less frequently ($p < .001$). In addition, the frail subgroup had a lower MMSE score ($p < .001$) and more depressive symptoms ($p < .001$) compared to the prefrail or nonfrail subgroups. Plasma cholesterol total levels were not statistically different among the three subgroups. Disability for mobility, IADL, and ADL activities at baseline was also significantly more frequent in the frail and prefrail subgroups in comparison to the nonfrail subgroup.

Disability

After 4 years, among participants without mobility disability at baseline, 44.4% of the nonfrail, 54.9% of the prefrail, and 68.2% of the frail persons developed mobility disability. Incident IADL disability was 8.0%, 12.6%, and 26.4% among nonfrail, prefrail, and frail subgroups, respectively, whereas

incident ADL disability was 0.7%, 1.0%, and 2.7% in (respectively) nonfrail, prefrail, and frail participants.

The unadjusted results showed that, in comparison to the nonfrail subgroup, the prefrail and frail subgroups had

Table 2. Proportions of Frailty Components by Sex in the Three-City Study

	All N = 6078	Men N = 2354	Women N = 3724
Frequency of Frailty Components (%)			
Shrinking	14.4	9.3	17.2
Weakness	12.7	9.1	14.9
Exhaustion	18.5	13.7	21.7
Slowness	20.8	20.6	21.0
Low physical activity	23.3	22.8	23.7
Number of Frailty Components (%)			
0	45.3	50.6	42.0
1	34.9	34.9	34.5
2	12.7	10.2	14.3
3	5.6	3.4	7.0
4	1.3	0.8	1.5
5	0.1	0.1	0.2
Total Frail (≥3 points)	7.0%	4.3%	8.7%

Note: Shrinking: Unintentional weight loss ≥ 3 kg or a body mass index ≤ 21 kg/m^2. Weakness: Answers "yes" to the question "Do you have difficulty rising from a chair?" Exhaustion: Self-reported, according to two questions from the Center for Epidemiological Studies-Depression scale. Slowness: Lowest quintile on timed 6-meter walking test (adjusted for sex and height). Low physical activity: Deny doing daily leisure activities (e.g., walking or gardening) and/or deny doing some sport activity per week.

Table 3. Incident 4-Year Disability by Frailty Status at Baseline (The Three-City Study)

	Mobility Disability $N = 3000$				IADL Disability $N = 5029$				ADL Disability $N = 5449$			
	Odds Ratio	95% CI*	p	p global	Odds Ratio	95% CI*	p	p global	Odds Ratio	95% CI*	p	p global
Unadjusted												
Frailty				<.001				.001				.001
Nonfrail (reference)	1	–	–		1	–	–		1	–	–	
Prefrail	1.52	1.31–1.76	<.001		1.76	1.45–2.13	<.001		1.21	0.71–2.07	.484	
Frail	2.68	1.58–4.54	<.001		4.10	2.96–5.66	<.001		10.76	6.30–18.37	<.001	
Adjusted												
Frailty				.002				<.001				<.001
Nonfrail (reference)	1	–	–		1	–	–		1	–	–	
Prefrail	1.33	1.13–1.57	<.001		1.43	1.15–1.78	.001		0.80	0.47–1.46	.556	
Frail	1.58	0.88–2.85	.131		2.10	1.41–3.11	<.001		3.20	1.57–6.52	.001	

Notes: Adjusted for age, sex, education level, income, smoking status, alcohol use, number of chronic diseases, self-reported health, Center for Epidemiologic Studies-Depression scale score (excluding the two questions used for the frailty definition), and Mini-Mental State Examination score. For incident instrumental activities of daily living (IADL) disability, odds ratios were also adjusted for baseline mobility disability. For incident basic activities of daily living (ADL) disability odds ratios were adjusted for baseline mobility and IADL disability.

CI = confidence interval.

significantly higher risks of incident disability for mobility and IADL However, for incident ADL disability, there were significant differences between frail and nonfrail participants, but not between prefrail and nonfrail participants (Table 3). Multivariate logistic regression analyses showed that, after adjusting for sociodemographic and health covariates, there were significant differences between the prefrail and nonfrail subgroups, but not between frail and nonfrail participants for the incidence of disability for mobility. For incident ADL disability, there were significant differences between frail and nonfrail, but not between prefrail and nonfrail participants, whereas for incident IADL disability, the relationship between prefrail and nonfrail, and frail and nonfrail subgroups remained significant (Table 3).

Table 4. Incident 4-Year Hospitalization by Frailty Status at Baseline (The Three-City Study)

	Hospitalization			
	Odds Ratio	95% CI	p	p global
Unadjusted				
Frailty				< .001
Nonfrail (reference)	1	–	–	
Prefrail	1.18	1.04–1.35	.012	
Frail	1.69	1.32–2.16	<.001	
Adjusted				
Frailty				.051
Nonfrail (reference)	1	–	–	
Prefrail	1.14	0.98–1.31	.081	
Frail	1.36	1.01–1.81	.042	

Notes: Adjusted by age, sex, education level, income, smoking status, alcohol use, number of chronic diseases, self-reported health, Center for Epidemiologic Studies-Depression scale score (excluding the two questions included in the frailty definition), Mini-Mental State Examination score, and baseline disability (mobility, instrumental activities of daily living, and basic activities of daily living).

CI = confidence interval.

Hospitalization

After 4 years of follow-up, 31.3% of the frail subgroup and 23.8% of prefrail participants had an incident hospitalization, compared to 20.3% of nonfrail participants.

The unadjusted regression analyses showed that prefrail and frail statuses were significantly associated with the incidence of hospitalization (Table 4). Multivariate logistic regression analyses showed that, after adjusting for all covariates mentioned above, including disability for mobility, IADL, and ADL at baseline, there were significant differences between frail and nonfrail, but not between prefrail and nonfrail subgroups associated to incident hospitalization; however, the overall association was only marginally significant.

Mortality

Incidence of death was 5.2% (316) at the 4-year follow-up. Cumulative mortality was 11.5%, 5.5%, and 4.4% in frail, prefrail, and nonfrail participants, respectively.

The unadjusted Cox proportional hazards model showed that, in comparison to being nonfrail, being frail at baseline significantly increased the risk of cumulative death at 4 years, whereas there were no significant differences between prefrail and nonfrail participants (Table 5). After adjusting for sociodemographic and health covariates (including disability for mobility, IADL, and ADL at baseline), frailty was no longer a statistically significant predictor of death (Table 5 and Figure 2).

DISCUSSION

The main purpose of this research was to describe the characteristics and prognosis of elderly participants defined as frail in a large sample of French community-dwelling people. The results obtained in this study partially replicate those previously described in North America and other countries of Europe regarding the relationship of frailty with adverse outcomes. Nonetheless, our results contribute to reinforce the predictive validity of the concept of frailty,

Table 5. Hazard Ratio of Death Estimates Over the 4-Year Follow-Up (The Three-City Study)

	Death			
	Hazard Ratio*	95% CI	p	p Global
Unadjusted				
Frailty				.048
Nonfrail (reference)	1	–	–	
Prefrail	1.17	0.92–1.50	.197	
Frail	1.54	1.09–2.17	.015	
Adjusted				
Frailty				.465
Nonfrail (reference)	1	–	–	
Prefrail	1.17	0.90–1.54	.234	
Frail	1.21	0.78–1.87	.397	

Notes: Adjusted for sex, education level, income, smoking status, alcohol use, number of chronic diseases, self-reported health, Center for Epidemiologic Studies-Depression scale score (excluding the two questions included in the frailty definition), Mini-Mental State Examination score, and baseline disability (mobility, IADL, and ADL).

*Cox proportional hazards model with delayed entry.

CI = confidence interval.

particularly for certain components of disability, and consequently the health status of the elderly population. The phenotype of frailty used in the present research was an independent predictor of the incidence of disability for IADL and ADL and of hospitalization, even adjusting for potential confounding variables. By showing the relationship between frailty and adverse health-related outcomes in a population having different lifestyle and eating habits, these findings partially resemble those reported in Italian, African American, and Mexican American populations where the same five components of frailty, as defined by Fried and colleagues, were considered (30–32). However, the prevalence of frailty has shown an important variability across populations (e.g., 8.8% for Italians, 12.7% for African Americans, or 20% for Mexican Americans), which could represent an independent association of race with frailty that is not explained by worse health, educational level, or lower socioeconomic status but rather by a different incidence and/or a different duration of this entity (32). This variability, as well as the severity of frailty among populations, could also explain the different incidence for

Four years:

Follow-up rate: 80.4%

n = 205 deceased
n = 444 refused evaluation
n = 430 lost to follow-up

Two years:

Follow-up rate: 88.9%

n = 111 deceased
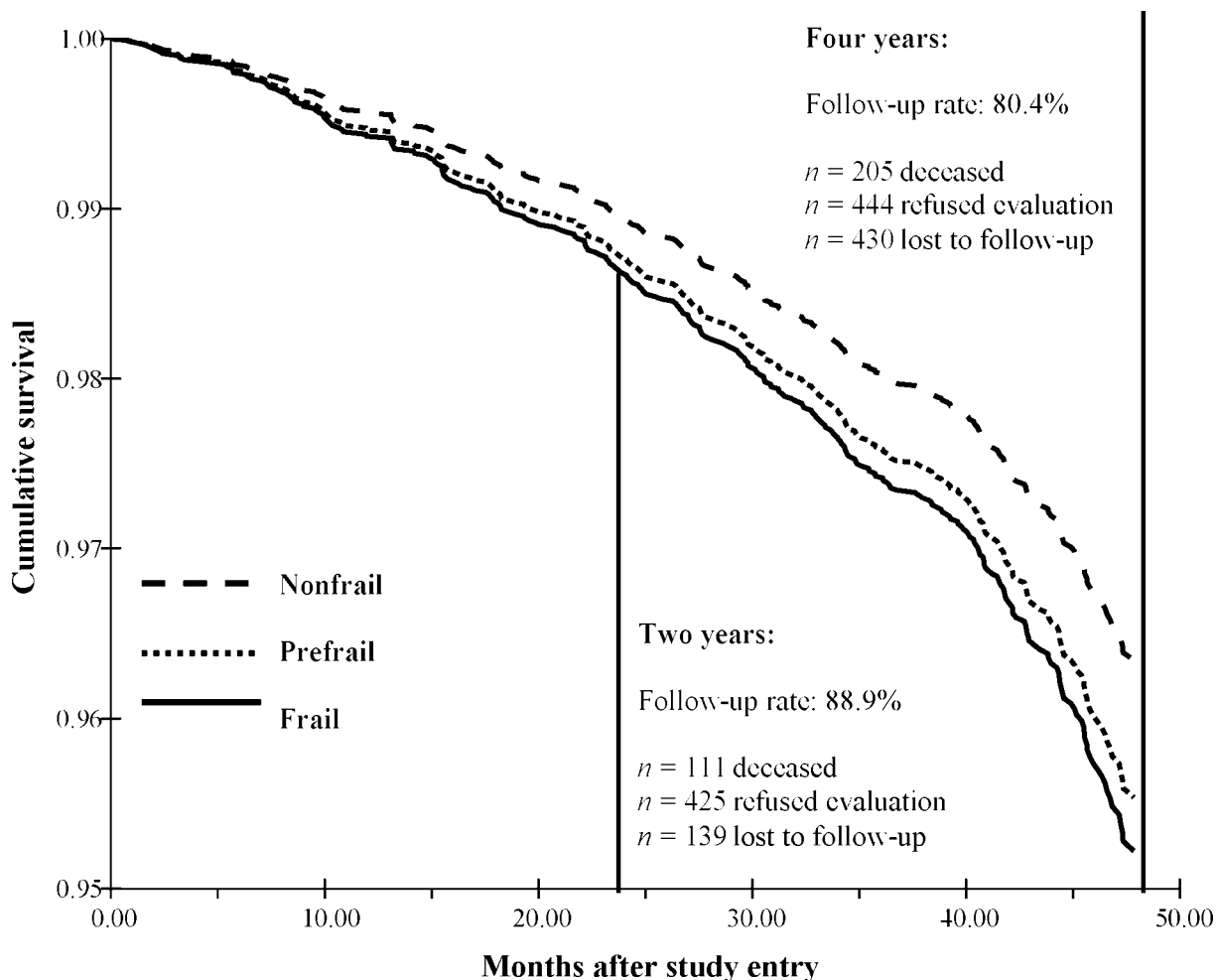n = 425 refused evaluation
n = 139 lost to follow-up

Figure 2. Survival curve estimate (adjusted) over the 4 years of follow-up according to frailty status at baseline. The Three-City Study.

certain adverse outcomes. A genetic basis for differences is also plausible.

The main limitation of this study may be the use of slightly different measures to define frailty criteria [because the measures originally used by Fried and colleagues (3) were not available in the 3C Study]. Using incomplete scales in multivariate analyses may be a limit also. In particular, with the exclusion of two items from the CES-D, the modified score slightly differs from the validated one. This score was computed to minimize the colinearity between frailty and mood. In addition, exclusion of participants with missing frailty scores (around 6.5% from the original sample) could induce a selection bias and affected the results, and a lack of power could explain the lack of relationship between all subgroups of frailty with the adverse outcomes in the adjusted analyses.

Nonetheless, despite these limits, the prevalence of frailty in elderly French persons (around 7%) was similar to that reported in other studies carried out in community-dwelling white people. Indeed, persons classified as frail were more likely to be older and female or to have more health problems. Besides the association with comorbidity and disability, adverse social conditions such as living alone or low income were also more frequent among frail and prefrail people. However, it is necessary to insist that frailty overlapped, but is not synonymous with, comorbidity and disability. Thus, as shown, not all frail participants were disabled at baseline, and not all who had a 4-year incident disability were frail at baseline. These findings support the hypothesis that frailty often precedes disability and that they are distinct entities. However, even if in this study the strength of the association between frailty and incident IADL and ADL disability was as previously reported, the phenomenon was not a statistically significant predictor of incident mobility disability after adjusting for multiple covariates. The exclusion of individuals with a prior mobility disability led to the exclusion of the most vulnerable persons, reducing substantially the risk for incident mobility disability.

In contrast, the amplitude of the confidence intervals in the significant strength of association between frailty and ADL disability in multivariate analyses may be explained by the low number of participants affected by this disability over time, possibly because of the general good health of participants at baseline or the relatively short period of follow-up (4 years).

Using data from the Women's Health and Aging Studies I and II, Bandeen-Roche and colleagues analyzed the number of categories or ''classes'' of frailty that are necessary to better capture its heterogeneity (two-class model: nonfrail and frail; three-class model: nonfrail, prefrail, and frail). The results showed that the two-category model is the most relevant. Considering our results showing that only one of the categories of frailty was associated with the incidence of mobility and ADL disability, and hospitalization, our study also suggests that the two-class model performs better than the three-class model. As it has been proposed, frailty may represent one extreme of a health continuum, and the inconsistency of an ''intermediate condition'' in predicting middle-term adverse outcomes could be explained by the longer duration of this status before ''true frailty'' and its consequences manifest.

In addition to physical aspects, other domains have to be considered to define frailty (33,34). Among the age-related conditions that could potentially be included, cognitive impairment is a good candidate. In this study, frail participants showed worse performance on the MMSE in comparison to prefrail and nonfrail subgroups. Although previously reported (35,36), the relationship between frailty and cognitive decline is largely debated. Both could share etiologic mechanisms, including chronic inflammation (37).

Fried's definition of frailty proves to be reproducible and relevant to predict different adverse outcomes through different populations showing its predictive validity. The use of a standardized phenotype will lead to a comparison between different populations and will possibly serve to identify etiological factors, components, or other correlates of frailty. This approach may be an acceptable option and awaits studies that consider the frailty concept as their principal objective of research. Nevertheless, important advances have occurred in the field with the proposal of methodological guidelines to include frail people in future research (38).

Despite the limits previously mentioned, this study has several strengths. Previous research in frailty has been conducted in France (39,40). However, this is the first one that uses a definition of frailty widely acknowledged to identify the affected individuals and to report its characteristics and prognosis. In addition, the study was conducted in a large population-based sample and had a prospective design.

Exploration of other possible dominions of frailty is necessary. Understanding the medical, biological, and environmental factors that contribute to the phenomenon of frailty is the goal of current research in the field (38). Elderly persons who are frail would benefit from complex, multidisciplinary care compared with usual care (41,42), which explains why efforts must be directed to detect this clinical state before irreversible disability or other adverse outcomes appear. Prospective research is required to ascertain whether intervention programs targeting frail persons may delay or reverse disability and loss of autonomy.

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