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Original Study

Prediction of Mortality by the Tilburg Frailty Indicator (TFI)

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A B S T R A C T

Objective: To predict mortality with the Tilburg Frailty Indicator (TFI) in a sample of community-dwelling older people, using a follow-up of 7 years.
Design: Longitudinal.
Setting and Participants: 479 Dutch community-dwelling people aged 75 years or older.
Measurements: The TFI, a self-report questionnaire, was used to collect data about total, physical, psychological, and social frailty. The municipality of Roosendaal (a town in the Netherlands) provided the mortality dates.
Results: Total, physical, and psychological frailty predicted mortality, with unadjusted hazard ratios of 1.295, 1.168, and 1.194, and areas under the receiver operating characteristic curves of 0.664, 0.671, and 0.567, respectively. After adjustment for age and gender, the areas under the curves for total, physical, and psychological frailty were 0.704, 0.702, and 0.652, respectively. Analyses using individual components of the TFI show that difficulty in walking and unexplained weight loss predict mortality.
Conclusions and Implications: This study has shown the predictive validity of the TFI for mortality in community-dwelling older people. Our study demonstrated that physical and psychological frailty predicted mortality. Of the individual TFI components, difficulty in walking consistently predicted mortality. For identifying frailty, using the integral instrument is recommended because total, physical, psychological, and social frailty and its components have proven their value in predicting adverse outcomes of frailty, for example, increase in health care use and a lower quality of life.

Frail older people, living independently in the community, have a high risk for disability,[1] hospitalization,[2] institutionalization,[3] lower quality of life,[4] and mortality.[5,6] It is therefore important to identify frail community-dwelling older people at an early stage and to carry out appropriate interventions so that these adverse outcomes of frailty can be prevented or postponed. A well-known instrument for assessing frailty in community-dwelling older people is the Tilburg Frailty Indicator (TFI),[7] developed on the basis of an extensive literature review and consultation of experts.[8,9] The TFI is a user-friendly self-report questionnaire, which aims to assess physical, psychological, and social frailty. Currently, the TFI has been translated into more than 10 languages, for example, Brazilian Portuguese,[10] Polish,[11] Chinese,[12] and Danish.[13] It has been reported that of 38 multicomponent frailty assessment instruments, including the frequently used phenotype of frailty,[2] and the Frailty Index (FI),[14] the TFI has the most robust evidence of reliability and validity.[15] Several studies have shown that the TFI can predict disability,[16–19] an increase in health care utilization,[17–19] and lower quality of life.[16,18,20]

Five studies have determined the predictive value of the TFI for mortality.[19,21–24] A Dutch study showed that frailty was associated

The authors declare no conflicts of interest

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with mortality within 3 years, adjusted for age, sex, and education, in a sample of 1042 community-dwelling people aged 65 years and older (odds ratio 3.27, $P < .001$).[22] In another Dutch cohort study including 2420 community-dwelling older people and with a 2-year follow-up, the area under the receiver operating characteristic curve (AUC) for predicting mortality by the TFI was 0.62, with a sensitivity of 80.6 and a specificity of 36.5.[23] In predicting mortality at 2 and 5 years, receiver operating characteristic curve analyses demonstrated AUCs of 0.74 and 0.73, respectively, using data of the Survey of Health, Aging and Retirement in Europe (SHARE), which included 27,527 community-dwelling adults (mean age 65.3 years, standard deviation 10.5).[24] The predictive validity of the TFI for mortality was also shown among 963 Brazilian people aged 60 years and older. Survival analysis of mortality according to frailty status during a 12-month follow-up period presented a hazard ratio of 2.72, adjusted for age and gender.[19] Finally, in a Danish sample consisting of 1328 acutely admitted older patients (≥65 years), frailty assessed with the TFI was associated with a higher risk of readmission or death within 6 months after discharge.[21]

The aforementioned studies, however, have some limitations for the prediction of mortality using the TFI. First, with regard to 2 of the aforementioned studies,[22,24] it should be noted that the original TFI was not used; the TFI was operationalized from data obtained by SHARE and the Longitudinal Aging Study Amsterdam (LASA).[22,24] Second, in the Danish, Brazilian, and the second Dutch study, the follow-up period can be considered as relatively short, being 6 months, 12 months, and 24 months, respectively.[19,21,23] Moreover, the Danish study was not focused on community-dwelling older people but included a specific target group (acutely admitted older patients).[21] The present study does not have any of these limitations. The aim of the present study was to determine the prediction of mortality by the TFI in a sample of community-dwelling people, using the original instrument and a follow-up period of 7 years.

Methods

Study Population and Data Collection

In June 2008, the TFI was sent to a sample of 1154 community-dwelling persons aged 75 years and older, randomly drawn from the register of the municipality in Roosendaal, a town of 78,000 inhabitants in the Netherlands. A total of 484 persons completed the questionnaire (42% response rate), which, in addition to the TFI, also contained measures for assessing disability and quality of life.[18,25]

Measures

Frailty

Part B of the TFI contains 15 components of frailty (total frailty): 8, 4, and 3 of these components belong to physical, psychological, and social frailty, respectively. The components of physical frailty are poor physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, poor hearing, poor vision, lack of strength in the hands, and physical tiredness. Psychological frailty consists of problems with memory, feeling down, feeling nervous or anxious, and unable to cope with problems. Finally, social frailty includes living alone, lack of social relations (loneliness), and lack of social support. The scores range from 0 to 15, 0 to 8, 0 to 4, and 0 to 3 for total and the physical, psychological, and social domains of frailty, respectively. Higher scores refer to a higher level of frailty.[7] Part A of the TFI includes 10 determinants of frailty. In this study, we present the data of 5 determinants: age, gender, marital status, ethnicity, and education (see Table 1), because these are well-known sociodemographic determinants of frailty.[8]

Table 1
Participant Characteristics at Baseline (N = 479)

Characteristic	n (%) or Mean (SD)
Sex	
Man	207 (43.2)
Woman	272 (56.8)
Marital status	
Married or cohabiting	238 (49.8)
Not married	45 (9.4)
Divorced	15 (3.1)
Widowed	180 (37.7)
Ethnicity	
Dutch	461 (96.6)
Other	16 (3.4)
Education	
No or primary	181 (38.1)
Secondary	221 (46.5)
Higher	73 (15.4)
Physical frailty components	
Poor physical health	138 (29.2)
Unexplained weight loss	36 (7.5)
Difficulty in walking	230 (48.1)
Difficulty in maintaining balance	166 (35.0)
Poor hearing	174 (36.6)
Poor vision	101 (21.4)
Lack of strength in the hands	164 (34.2)
Physical tiredness	217 (45.4)
Psychological frailty components	
Problems with memory	46 (9.6)
Feeling down	192 (40.2)
Feeling nervous or anxious	148 (31.0)
Unable to cope with problems	71 (15.0)
Social frailty components	
Living alone	229 (47.8)
Lack of social relations	282 (59.0)
Lack of social support	78 (16.4)
Mortality, death	162 (33.8)
Continuous variables, mean (SD)	
Age	80.3 (3.8)
Total frailty	4.7 (3.0)
Physical frailty	2.5 (2.1)
Psychological frailty	0.9 (1.1)
Social frailty	1.2 (0.9)

Mortality

In August 2015, referring to a follow-up period of approximately 7 years, the municipality of Roosendaal provided the mortality dates of the participants who completed the questionnaire in 2008.

Statistical Analysis

We used descriptive statistics to describe the baseline characteristics of the participants. Categorical variables were presented as counts and percentages. Continuous variables were presented as means with standard deviation. We defined a time-to-event outcome using the data of the mortality of the participants. The time in days was set to 0 at the time point the first participant died, and was set to 2613 for participants who were not dead.

In 2 sections, we first predicted mortality with a continuous frailty score (total, physical, psychological, or social as is common in studies using the TFI, and with a dichotomous frailty score using the defined cutoff points 5, 3, 2, and 2 for total, physical, psychological, and social frailty, respectively,[7,26] as this is how the TFI is commonly used in practice). In the subsequent section, we also predicted mortality with individual frailty components, examining which components contribute most to the (possible) predictive success of a frailty domain. In this last analysis, only the frailty components were included, with a bivariate P value $< .20$.[27] Finally, all aforementioned analyses were also conducted by adjusting for age and gender, as these are strongly associated to mortality. Before examining the prediction

of mortality by individual components of total frailty, we imputed data for the missing values in the frailty components using the MICE package within the R software (m = 5, method: logreg).[28]

For all analyses of survival, we used Kaplan-Meier analyses and Cox regression analyses to calculate hazard ratios (HRs) with 95% confidence intervals (CIs). The Kaplan–Meier survival curves with respect to subgroups were compared using the log-rank test. The predictive performance of the models was measured using the AUC. An AUC >0.7 was considered as an indication for good predictive performance.[27] For all analyses, we considered a *P* value < .05 as significant. For the analyses, we used R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria).

Ethical Considerations

For this study, medical ethics approval was not necessary, as particular treatments or interventions were not offered or withheld from respondents. The integrity of respondents was not encroached on as a consequence of participating in this study, which is the main criterion in medical-ethical procedures in the Netherlands.[29] Informed consent in relation to detailing the study and maintaining confidentiality was observed.

Results

Participant Characteristics

As in a previous study, the data of 5 participants (1.0%) were left out of the analyses as they had too many missing values.[18] The analyses using frailty domain scores were carried out on the data of 455 participants (92.9%) with full data on all frailty components. The analyses using frailty components were carried out on the data of all 479 participants after imputing the missing data on components (0.54%).

Of the 479 participants at baseline, the mean age was 80.3 years (standard deviation = 3.8); 272 (56.8%) were women and 238 (49.8%) were married or cohabitating. The prevalence of frailty was 47.1%. Lack of social relations was the most prevalent component of frailty (282; 59.0%). Within the follow-up period of 7 years, 162 individuals died. See Table 1 for the descriptive statistics of the participants.

Prediction of Mortality by Total, Physical, Psychological, and Social Frailty

Table 2 presents the HRs for the total, physical, psychological, and social frailty scores with associated 95% CIs, *P* values, and AUCs, both unadjusted and adjusted for age and gender. Total, physical, and psychological frailty scores predicted mortality (all *P* values < .01), even after adjustment for age and gender.

Social frailty did not predict mortality—the AUCs varied (unadjusted) from 0.551 (social frailty) to 0.671 (physical frailty).

Prediction of Mortality by Total, Physical, Psychological, and Social Frailty Based on Cutoff Points

Figure 1 presents the survival plots distinguishing frail from nonfrail older people using the defined cutoff points. The comparison of the survival plots with respect to the subgroups, defined by the cutoff points of total, physical, psychological, and social frailty using the log-rank test, showed *P* values of < .001, <0.001, 0.030, and 0.30, respectively. HRs and AUCs based on frailty cutoff scores showed (again) that total, physical, and psychological frailty predicted mortality (see Table 2).

Prediction of Mortality With All 15 Individual Components of Frailty

We excluded 4 components (poor hearing, poor vision, feeling down, and living alone) from the multivariate analyses because of *P* >.20 for these components in the bivariate analyses (results for bivariate analyses not shown). The Cox regression model with the 11 remaining components showed unadjusted and adjusted (for age and gender) AUCs of 0.716 and 0.747, respectively. Two components (unexplained weight loss and difficulty in walking) predicted mortality (unadjusted); in the adjusted model, these 2 components and lack of strength in the hands and physical tiredness predicted mortality. For more details, we refer to Table 3.

Discussion

Many studies have shown that frailty is associated with premature death in community-dwelling older people.[5,6] At present, only 5 studies have used the TFI for the prediction of mortality,[19,21–24] of which only 1 used the original instrument in Dutch community-dwelling older people with 2-year follow-up.[23] The aim of our study was to determine the predictive value of the TFI for mortality in a Dutch sample of 479 community-dwelling older people with a longer follow-up period (7 years).

Total, physical, and psychological frailty predicted mortality, with unadjusted HRs of 1.295, 1.168, and 1.194 and AUCs of 0.664, 0.671, and 0.567, respectively, and age-adjusted and gender AUCs were somewhat higher (0.704, 0.702, and 0.652, respectively). The unadjusted AUC for total frailty is comparable with the AUC of the TFI in the previously mentioned similar study, using a follow-up of 2 years (0.664 vs 0.620),[23] and with the AUCs of the frailty phenotype[2] (0.65), the Groningen Frailty Indicator[30] (0.64), and the FI[14] (0.64).[23] The AUCs of all these frailty instruments had higher scores in SHARE using a follow-up of 2 years, ranging from 0.72 (Groningen Frailty Indicator)

Table 2
Prediction of Mortality Using Frailty (Total Scores and Cutoffs): HRs and AUCs (*P* Values and CIs)

Frailty	Unadjusted					Adjusted for Age and Gender				
	HR	95% CI	*P* Value	AUC	95% CI	HR	95% CI	*P* Value	AUC	95% CI
Based on scores										
Total	1.168	1.109, 1.231	<.001	0.664	0.611, 0.718	1.169	1.109, 1.233	<.001	0.704	0.651, 0.757
Physical	1.295	1.200, 1.398	<.001	0.671	0.619, 0.724	1.278	1.182, 1.383	<.001	0.702	0.651, 0.754
Psychological	1.194	1.047, 1.363	.008	0.567	0.515, 0.619	1.224	1.071, 1.398	.003	0.652	0.599, 0.706
Social	1.159	0.976, 1.376	.09	0.551	0.499, 0.602	1.170	0.976, 1.403	.09	0.641	0.588, 0.694
Based on cutoffs										
Total	2.265	1.617, 3.173	<.001	0.627	0.579, 0.675	2.313	1.628, 3.285	<.001	0.687	0.634, 0.741
Physical	2.218	1.604, 3.068	<.001	0.622	0.575, 0.669	2.143	1.534, 2.995	<.001	0.678	0.625, 0.730
Psychological	1.428	1.030, 1.980	.032	0.552	0.506, 0.597	1.526	1.096, 2.123	.012	0.647	0.593, 0.700
Social	1.187	0.871, 1.619	.278	0.533	0.485, 0.580	1.150	0.831, 1.589	.399	0.635	0.582, 0.688

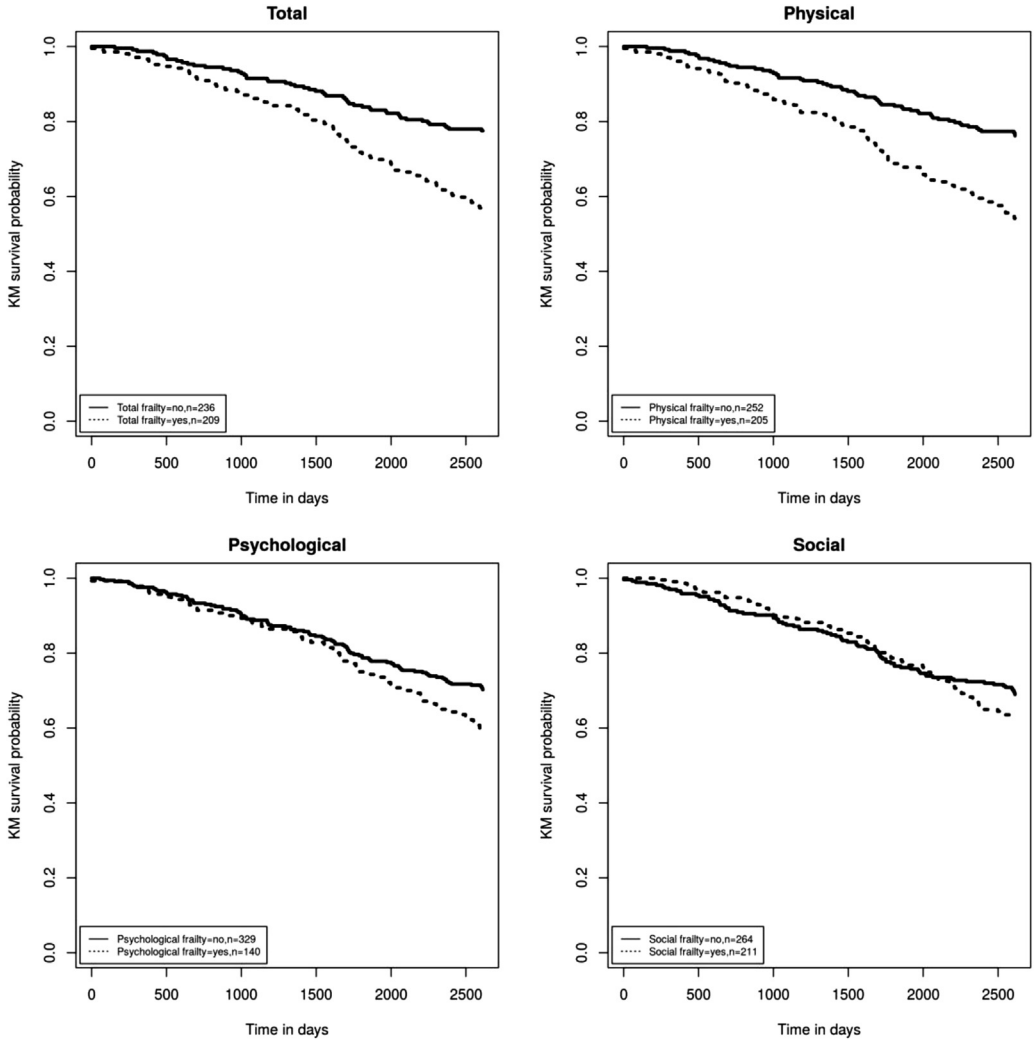

Fig. 1. Kaplan-Meier (KM) survival curves distinguishing frail from nonfrail older persons.

to 0.77 (FI), and a follow-up of 5 years, ranging from 0.70 (Groningen Frailty Indicator, frailty phenotype) to 0.75 (FI).[24]

The present study is the first to examine AUCs for mortality by the individual frailty domains, so a comparison of these AUCs with other studies is unfortunately not possible. In our study, the AUC of physical frailty was comparable with the AUC of total frailty. Social frailty did not predict mortality significantly. In a previous Dutch study carried out by the Netherlands Institute for Social Research, social frailty, assessed with the subscale of the TFI, did not increase the risk of death either.[31] We, therefore, conclude that the physical frailty domain is mostly responsible for the prediction of mortality. However, we do not recommend only using this domain for prediction, as other studies

Table 3
Prediction of Mortality Using Frailty Components: HRs (*P* Values and CIs)

Frailty Component	Unadjusted			Adjusted for Age and Gender		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Poor physical health	1.169	0.786, 1.737	.44	1.183	0.789, 1.773	.42
Unexplained weight loss	1.917	1.157, 3.178	.012	1.804	1.078, 3.020	.025
Difficulty in walking	2.066	1.367, 3.122	.001	1.942	1.274, 2.960	.002
Difficulty in maintaining balance	1.439	0.986, 2.099	.06	1.415	0.963, 2.081	.08
Lack of strength in the hands	0.683	0.464, 1.005	.05	0.659	0.441, 0.986	.043
Physical tiredness	1.430	0.961, 2.128	.08	1.512	1.008, 2.267	.046
Problems with memory	1.565	0.990, 2.472	.06	1.460	0.910, 2.343	.12
Feeling nervous or anxious	0.906	0.626, 1.311	.60	0.905	0.614, 1.332	.61
Unable to cope with problems	1.110	0.721, 1.711	.64	1.248	0.798, 1.952	.33
Lack of social relations	1.327	0.931, 1.894	.12	1.325	0.917, 1.914	.13
Lack of social support	1.212	0.805, 1.823	.36	1.155	0.753, 1.772	.51

All components were entered into the model simultaneously.

show that the other frailty domains (eg, psychological, social) do predict other future adverse outcomes, such as an increase in the use of care and a lower quality of life.[18,20]

The AUC, using the individual components of the TFI for total frailty, was higher than the AUC determined with the total score (unadjusted: 0.716 vs 0.664). Consequently, if the researcher's aim is to identify very specific predictors of adverse outcomes, we recommend analyzing their associations with individual frailty components, but only in large samples when statistical power is less of an issue (eg, with a sample size of 1000 or more, small effects can be detected with power at least equal to 0.8 with $\alpha = 0.01$). In smaller samples, and for practical purposes, we recommend using the total frailty score for predicting adverse outcomes, or the 3-domain scores.

The analyses using individual components of the TFI suggest that the 2 components difficulty in walking and unexplained weight loss predict mortality, even after adjustment for age and gender, and the effects of other components. Difficulty in walking is a well-known predictor of mortality. A prospective cohort study among British men, with a follow-up period of 2 up to 4 years, demonstrated that gait speed predicted mortality, with HR 2.90 (95% CI 1.84, 4.56) (physical performance) and HR 2.98 (95% CI 1.91, 4.66) (self-report).[32] In addition, low gait speed, assessed with the 6-m walking speed test, predicted mortality among 1176 older people living in the community, with an AUC value of 0.723.[33] Finally, a study carried out in a large sample of inhabitants of Latin America, India, and China, found that slow walking speed predicted mortality, with 47,438 person-years of follow-up.[34]

Unexplained weight loss is, like difficulty in walking, weakness (decreased grip strength), exhaustion, and low physical activity, a component of the phenotype of frailty,[2] and a frequently used measure of physical frailty. A systematic review and meta-analysis of prospective cohort studies, including 35,538 older people and 7994 deaths, revealed that frail older people, defined according to the phenotype of frailty, had a higher risk of mortality compared with prefrail and robust older people.[35] The aforementioned study among British men showed that unintentional weight loss, assessed by physical examination and subjective assessment (self-report), predicted mortality, with HR 3.88 (95% CI 2.44, 6.16) and HR 3.14 (CI 2.02, 4.87), respectively.[32] In another study, men, as well as women (N = 4926), had higher mortality rates for weight loss (likely involuntary) with a ≥10-year follow-up period after adjustment for age, lifestyle, and medical factors.[36] In addition, a systematic review and meta-analysis including 15 observational studies concluded that unintentional weight loss had a significant effect on all-cause mortality.[37] However, findings of a randomized controlled trial showed that intentional weight loss was not associated with increased all-cause mortality over 12 years of follow-up in older people with overweight or obesity.[38]

Another reason to be reluctant to interpret the effect of unintended weight loss is that it is not statistically significant after adjusting for multiple testing with the Bonferroni correction [ie, the *P* values (0.012 and 0.025) exceed 0.05/10 = .005]. This also holds for the effects of 2 physical components lack of strength in the hands and physical tiredness, which were only just statistically significant in the analysis adjusted for age and gender. Based on our findings and previous studies, we therefore recommend further research focusing on the role of weight loss, both unintentional and intentional, in the prediction of mortality among older people, especially stratified for gender and groups related to body mass index, but also on the effects of lack of strength in the hands and physical tiredness.

With regard to the predictive validity of the physical components of the TFI, it would be relevant to compare these findings with physical tests in the same population. Future research could examine if physical tests are necessary to be performed for the prediction of mortality, or that a self-report questionnaire such as the TFI is sufficient. This has been shown, for example, in the prediction of indicators of health care utilization (eg, visits to the general practitioner, receiving personal care, receiving nursing).[17]

Of the 15 components of the TFI, 4 were not included in the multivariate analyses: poor vision, poor hearing, feeling down, and living alone. However, removing these components from the TFI, on the basis of this study, is not recommended. The inclusion of sensory difficulties into a screening instrument such as the TFI has major consequences in terms of prevalence and the prediction of other adverse outcomes (eg, hospitalization).[39] The same applies for feeling down and living alone; for example, both frailty components are associated with lower quality of life in older people.[20,40]

Some limitations of this study should be noted. First, the sample consisted solely of people living in the municipality of Roosendaal; the generalizability of the findings can therefore be questioned. Second, the TFI is a frailty instrument based on self-report, so frailty is subjectively determined. However, the construct validity of the TFO has been extensively evaluated using objective measures. In addition, self-reported information concerning the components of the phenotype of frailty demonstrated superior predictive and discriminatory ability compared with objective measures of these components.[32] A strength of the present study is that the sample consisted of community-dwelling older people aged ≥75 years and older at baseline. Moreover, the mortality dates were correct, as they are derived from the register of the municipality, and the period of follow-up was long (7 years), in particular for this target group and in comparison with the other studies focusing on the prediction of mortality in community-dwelling older people by the TFI.[19,22–24]

Conclusions and Implications

In conclusion, this study has shown the predictive value of the TFI for mortality in community-dwelling older people. Our study demonstrated that both physical and psychological frailty predicted death. Of the 15 individual TFI components, difficulty in walking consistently predicted mortality. However, for identifying multidimensional frailty, consisting of physical, psychological, and social frailty, it is important to use the integral instrument because all domains have proven their value in predicting other adverse outcomes of frailty, for example, disability, increase in health care use, and a lower quality of life.

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