Mathematical modelling of frailty, dependency and mortality in a 70-year-old general population.

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ABSTRACT
Due to the aging of the world population, a better functional capacity of the elderly is needed. The importance of detecting people at risk of frailty, dependence and death to fulfill an individualized approach. There are models that uses frailty indices, but none that use the Frail-VIG Index, based on the comprehensive geriatric assessment. Three predictive models of frailty, dependency and mortality for 70-years-old in general population are presented. The risk factors for developing frailty or dependency are female gender, chronicity level 2 or 3, and marriage. For mortality the risk factors are male gender, low educational level and being frail according to frail-VIG index. In conclusion, the health actions to prevent frailty and dependence should focus on reducing the chronicity level, especially in women. To delay mortality, an individualized approach should be implemented in frail people.Further studies are needed to determine other health and social risk factors.

KEYWORDS
Prognostic factors, Frailty, Dependence, Mortality, Survival analysis, Nomogram, Prediction model.

1. Introduction

The ageing of the world's population is an obvious fact. Life expectancy at birth is projected to increase from 71 years in 2021 to 77 years in 2050 [20]. The proportion of people aged 65 or over is projected to increase globally between 2022 and 2050, from 10% to 16%. In 2050, one in every four persons in Europe and Northern America could be aged 65 years or over. Faced with these projections, countries with aging should take steps to adapt their public health programs and health care systems to this problem, including universal health care and long-term care systems. The current challenge is to act on modifiable factors that can be intervened, like frailty, to promote the maintenance of functional capacity. In this way, the appearance of disability or dependency would be reduced [37].

There are multiple definitions of frailty, but does not yet have an internationally recognized standard definition. The Advantage Join Action considers frailty like a clinical state in a person that increases his vulnerability to develop adverse outcomes

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when exposed to a stressor [9]. Frailty is a predictor of mortality, disability, among other adverse health outcomes [42]. Frailty has not only been linked to an increased risk of all-cause mortality, but is also a strong predictor of mortality from specific causes such as cardiovascular disease, cancer, and respiratory diseases in adults living in the community [39].

The two most known definitions of frailty are the frailty phenotypic model proposed by Fried et al in 2001 [19], and the deficit accumulation model developed by Rockwood in 2005 [43]. The frailty phenotype [19] is a clinical syndrome in which three or more of the following criteria are present: unintentional weight loss (10 lbs in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity. The frailty indices are derived from the deficit accumulation definition [43], that includes social assessment, comorbidity... among others elements, and views frailty as a continuum. The cumulative deficit model is consider more accurate predictor of mortality than phenotype frailty [32]. In 2016, Amblàs et al [3] developed the Frail-VIG index (see Appendix A), a frailty index based on the comprehensive geriatric assessment (CGA, VIG "valoración geriátrica integral" in Spanish). This index contains 22 simple questions that assess 25 different deficits, recorded during the usual clinical evaluation process. Any measures of frailty are recognized as a gold standard [8], but CGA is considered the best system for frailty management in elderly people. Because of that, frail-VIG index is a useful tool for Primary Health Care in order to assess general population. The frail-VIG index presents an optimal capacity to predict mortality [3–5]. Its construct validity [10, 54, 56, 57], reliability and feasibility [54] have been studied. Frail-VIG index has been compared to SPPB [10], Fried's phenotype [54] and the Clinical Frailty Scale [38, 54]. The relationship of the frail-VIG index with constructs related to frailty, such as functional capacity [10], and quality of life [56] has been studied.

Various investigations have studied frailty risk factors, measuring frailty with the Fried's phenotype [36, 41], or by deficit accumulation model [46]. There are few predictive models of frailty in the literature. Li et al [33] developed a frailty prediction model with many variables, and it is a handicap for the implementation in daily clinical practice. Dong et al [17] developed a nomogram to predict the progression of frailty. Regarding the predictive models of functional status, Van Grootven et al [23] in their systematic review considered that no model could be recommended for implementation in clinical practice, but the most promising are those that consider frailty. There are some predictive models of mortality like the Chen et al [13], Lund et al [35], or Gu et al [24] in the oldest old. There is a problem to compare the investigations: in each study they create their own frailty index, usually using the Searle's methodology [45].

Zamudio et al showed in his study that frailty and the two stages of disabilities (firstly disability in instrumental and then disability in basic activities of daily living) follow a hierarchy along a continuum [58]. For this reason, it is important to detect frailty prior to dependency: the decline is dynamic, with potential reversibility, "not an inevitable trajectory to death" [22]. Disability in essential ADL (activities of daily live) is potentially reversible in newly disabled older people, but those who recover are at high risk for recurrent disability [27].

There are many reasons to predict frailty, dependency and mortality. Firstly, to carry out preventive actions necessary to improve people's future quality of live, from childhood. Knowing the risk of these adverse outcomes can help the patient take responsibility for his health. Health professionals could individualize the therapeutic approach, always taking into account the decisions of the patients. It is important to know the dependency and mortality risk to be able to educate the families and prepare

for possible needs that patients may have. The health system must be adapted to the needs of people with dependency. Furthermore, there must be a national economic forecast for the increase in costs that will occur in the future.

The objective of the study is to develop a predictive model of frailty, dependency and mortality related with personal characteristics in population aged 70 years from community dwelling, and to stablish prognostic factors of these outcomes. The clinical variables that we are going to study are: frailty using the frail-VIG index, chronicity level and functional capacity measured with the SPPB.

2. Methods

2.1. Study Design and Study Population

This is an observational population-based study, in people aged 70 year or over from two lists of general practitioners of the Moncada's Primary Health Care. Sociodemographic data were collected: gender, marital status, educational level and number of cohabitants. Dependence was measured with the Barthel Index, and frailty with the Frail-VIG Index [3] and the Short Physical Performance Battery (SPPB) [25]. We requested the chronicity level to the Conselleria de Sanitat of Valencia, which classifies the chronicity in four categories: level 0, level 1, level 2 and level 3, meaning healthy people, chronic patients with low, moderate and high complexity, respectively.

The Barthel Index is a questionnaire that measures performance in activities of daily living. It was categorized in the next groups, based in the Shah criteria [47]: no dependent (IB$\geq$95), mild dependency (IB 90-65), moderate-severe dependency (IB 25-60), and absolute dependency (IB$\leq$20). Frail-VIG Index is a questionnaire with 22 items that assess 25 deficits classified in eight domains: functional, nutritional, cognitive, emotional, social, geriatric syndromes, severe symptoms and diseases. The range goes from 0 to 1, and categorizes frailty in: no frail ($<$0.20), mild frailty ($0.20-0.35$), moderate frailty ($0.36-0.50$) and severe frailty ($>$0.50). The SPPB [25] assess the lower extremity physical performance status. It consist in three test: test of standing balance (tandem, semi-tandem and side-by-side stands), walking speed test, and the ability to rise from a chair test. The range goes from 0 to 12. The cut of point we established was "seven", because it was the best cut-off point identified in the Fradea study [1]. Frail-VIG index includes the Barthel Index, for that reason we calculated a new cut-off point of the Frail-VIG Index without the Barthel Index item. We used Frail-VIG Index without the Barthel index item when it is evaluated as predictive factor of dependency. We collected mortality data in May 2022, three years after the first data collection in February 2019.

This study was approved by the "Ethic Investigation Corporative Committee of Primary Health Care from the Comunitat Valenciana", in 01/31/2019, registration number 18/10. Participants or representatives were informed and signed the consent.

Data were anonymized, and the study complied with the data protection regulation "Organic Law 3/2018, of December 5, concerning protection of personal data and guarantee of digital rights".

2.2. Survival Analysis

The main objective of this paper is to establish prognostic factors of death related to personal characteristics, and also dependency and frailty in population over 70 years

old. *Survival analysis* techniques are used to analyze data in the form of times until the occurrence of a specific event or *end-point*, with all individuals starting from the same *time origin*. This type of data is referred to as *time-to-event* data or *survival data*. In some cases, the event of interest may not be observed in an individual, such as when the observation period ends before the event occurs. This is known as *censored data* or in particular *right-censored* if the study concludes before the event can be observed. Survival analysis allows for the analysis of this type of incomplete or censored data. In this study, the common time origin was set at the age of 70 years old, and three different events or endpoints were considered for analysis:

(1) Dependence, measured with the Barthel Index (*time until dependece* or *time free of dependence*).
(2) Frailty, measured with the Frail-VIG index (*time until frailty* or *time free of frailty*).
(3) Death (*survival time*), taking into account dependence and frailty information.

Let T be the random variable associated with the time until the event under study occurs (dependence, frailty or death). Then the *distribution function* of T is defined by

$$F(t) = P(T < t) = \int_0^t f(u)du, \tag{1}$$

where $f(t)$ is the *probability density function* of the random variable T. The *survivor function*, $S(t)$, is defined to be the probability that a person suffers the event at a time beyond some specified time t, and so is computed through

$$S(t) = P(T \geq t) = 1 - F(t). \tag{2}$$

Survival data or time-to-event data is commonly summarized using survivor functions. In this study, the Kaplan-Meier estimator was utilized to estimate the survivor functions. To compute this estimator let us suppose there are n individuals in the database with observed times to event $t_1, t_2, \ldots t_n$. Some of these collected times may be censored data, resulting in $r < n$ different observed times to event (non-censored data). If $t_{(1)} < t_{(2)} < \ldots t_{(r)}$ are these r ordered times, n_j denotes the total of individuals who are free of the event just before time $t_{(j)}$ for $j = 1, 2, \ldots r$, and d_j denotes the number of individuals who suffer the event at this time, then the Kaplan-Meier estimate of the survivor function for this group of individuals is given by

$$\hat{S}(t) = \prod_{j=1}^{k} \left(\frac{n_j - d_j}{n_j} \right), \tag{3}$$

for $t_{(k)} \leq t < t_{(k+1)}$, $k = 1, 2, \ldots r$ and with $\hat{S}(t) = 1$ for $t < t_{(1)}$.

When estimating the survivor function for various groups of survival data, such as different categories of a single explanatory variable, one method of comparing the resulting functions is to plot the corresponding estimated curves on the same axes. Subsequently, the log-rank test can be utilized to test the null hypothesis of equality

among the depicted survivor functions. The log-rank test is a large-sample chi-square test that measures the discrepancy between the observed and expected failures as an indicator of the contrast between the actual data and the null hypothesis [14]. In instances where the test is employed to compare three or more groups and indicates a statistically significant difference among the estimated curves, a pairwise log-rank test (two-to-two comparison) is conducted to analyze the significant difference between all curves and recode the explanatory variable by joining the groups statistically equivalent. A p-value lower than 0.05 obtained from the test is considered significant.

This univariate analysis enables us to identify potential prognostic factors associated with dependency, frailty, and death. The subsequent step involves analyzing the relationship between the time to the event (dependence, frailty, and death) and the explanatory variables that exhibit joint statistical significance. To achieve this, the Cox regression model was utilized. The relationship is explored by examining the risk function, which is defined as the instantaneous event rate or intensity rate, given by the limit

$$h(t) = \lim_{\delta t \to 0} \frac{P(\, t \leq T \, < \, t + \delta t \,|\, T \geq t)}{\delta t} \tag{4}$$

Using the definition of conditional probability, the risk function is related to the survivor function through the expression $h(t) = f(t)/S(t)$. Let us suppose that the risk of an event at a time t depends on the value of p explanatory variables $X_1, X_2, \ldots X_p$. Let us denote $x_{1i}, x_{2i}, \ldots, x_{pi}$ the values of these explanatory variables at time t for the *i-th* individual. Then, the Cox regression model describes the risk for this individual as

$$h_i(t) = exp(\beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_p x_{pi}) h_0(t), \tag{5}$$

where $h_0(t)$ is called the *baseline hazard function* and represents the risk of the reference individual. This individual can be defined as the one with all coded explanatory variables x_{ji}, set to zero for $j = 1, 2 \ldots, p$ or for continuous variables, it can be the individual with the average values of the variables. The β_i for $i = 1, 2, \ldots, p$ are the parameters of the model to be estimated. Note that the risk ratio between the *i-th* individual and the reference individual, is constant and independent of the time: $exp(\beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_p x_{pi})$. Thus, the exponential of a parameter associated with a particular variable gives us information about the change in risk with respect to the risk of the reference individual when the rest of the effects or variables remain equal. The coefficients β of the model can be estimated using the *method of maximum likelihood*. The *likelihood* function of the sample data is defined as the joint probability of the r observed event times $L(\beta) = L_1 L_2 \ldots L_r$, where the term L_j for $j = 1, 2, \ldots r$ represents the contribution of the *j-th* event time to the likelihood. It is calculated as the ratio between the single risk of the individual who got the event at time t_j, and the sum of the risks of all individuals who are still at risk at this time t_j. By maximizing the *likelihood function* $L(\beta)$ or the *log-likelihood function* $\log L(\beta)$, we can obtain the maximum likelihood estimates of the β-parameters. Alternatively, these estimates can be obtained by minimizing the $-2 \log L(\beta)$.

The value of $-2 \log \hat{L}(\beta)$ for a given dataset is then a measure of the agreement between the model and the data. Here, $\hat{L}$ represents the likelihood computed by re-

placing the estimated parameters, $\hat{\beta}$. A smaller value of $-2\log\hat{L}(\beta)$ indicates a better fit of the model to the data. This value can be utilized to compare models that have been fitted to the same dataset. The three selected models (risk of dependence, frailty or death) were obtained using a variable selection strategy suggested in [14] based on the comparison of nested models by examining the change in the value of the statistic $-2Log\hat{L}$. The methodology follows five steps for the selection model:

(1) By fitting all the univariate models and testing the significant change in $-2\log\hat{L}(\beta)$ with respect to the null model, we can detect the variables that significantly affect the time-to-event.
(2) All significant variables from the first step are fitted together. Then, they are individually removed one by one, and the change in $-2\log\hat{L}(\beta)$ is checked. Variables that are non-significant in the presence of others are not retained in the model.
(3) Variables that were not considered significant in the first step are analyzed again to determine if they become significant in the presence of variables included in the model.
(4) After obtaining the model in Step 3, the second step is repeated. If any variable is removed, then Step 3 needs to be repeated.
(5) Once a model is obtained, it is necessary to examine all possible interactions between the variables included in the model.

The resulting models to predict dependency, frailty, and death were depicted as nomograms. Nomograms are graphical tools that assign a score to each level of each variable in the model to show the joint contribution of all the prognostic factors for an individual. Nomograms were built to predict the probabilities of being free of dependency, being free of frailty, and surviving at different ages (75, 85, and 90 years old).

Harrell's concordance index (C-index) [28] was used to asses models accuracy (discrimination). The C-index is the non-parametric version of the Area Under the Curve (AUC) that can take into account censored data. This index represents the probability that, out of two randomly selected individuals, the person with worse prognostic factors will experience the event before the other individual. It ranges from $C = 0.5$ (random discrimination) to $C = 1$ (perfect discrimination).

The statistical analysis for this study was conducted using R [52] with specific libraries: *survival*, *rms* [29] and *OptimalCutpoints* [34].

3. Results

The database consists of detailed information on 416 patients aged 70 years or older. Mean age ($\pm$ S.D.) of patients was 78 $\pm$ 6.16 years old. 54 (13%) of the 416 patients died at a mean age of 84.31 $\pm$ 6.79 years old. The main characteristics collected of the patients are shown in Table 1.

Table 2 presents the result of the univariate analysis, where the variables significant to be prognostic factors of dependence, frailty and death are identified. The results obtained establish *gender*, *educational level* and *Barthel index* as prognostic factors of death, *marital state* and *chronic desease level* were detected as prognostic factors of the three events under study: dependence, frailty and mortality. *Number of cohabitants* affects to the time free of frailty of a patient and finally, *Frail-VIG index* was iden-

Table 1. Patients Characteristics.

	Number (%)
Gender	
Male	180 (43.3)
Female	236 (56.7)
Marital state	
With partner	246 (59.1)
No partner	170 (40.9)
Educational level	
No Read/Write	30 (7.2)
Primary studies	335 (80.5)
High school or higher	51 (12.3)
Number of cohabitants	
Live alone	87 (20.9)
2 cohabitants	232 (55.8)
3 or more cohabitants	97 (23.3)
Chronicity level	
Healthy	15 (3.6)
Low complexity chronic disease	161 (38.7)
Medium complexity chronic disease	171 (41.1)
Severe complexity chronic disease	69 (16.6)
Barthel index	
No dependent	305 (73.3)
Dependent	111 (26.7)
Frail-VIG index	
No frail	294 (70.7)
Frail	122 (29.3)
SPPB index	
No frail	294 (74.2)
Frail	102 (25.8)

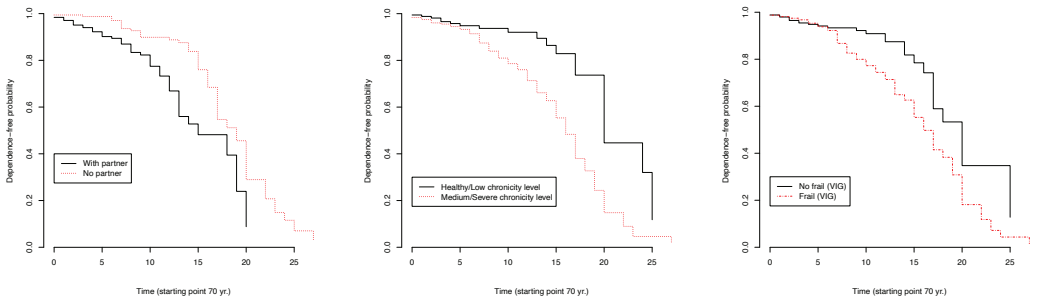
tified as prognostic factor for dependency and death. The pairwise log-rank allowed recode the levels of the variables in significantly different. Kaplan-Meier estimates are plotted for the significant variables and its recoded levels for the three end-points: dependence-free functions in Figure 1, frail-free functions in Figure 2 and survivor functions in Figure 3. The *Chronicity level* variable was coded as two levels: healthy or low complexity chronic disease level and moderate/severe complexity chronic disease level when it was evaluated as predictive factor of dependence or frailty. In contrast, when it was evaluated as predictive factor of survival, the two levels with significantly different survivor curves were: chronic disease without severe complexity level versus chronic disease of severe complexity level. The variable *educational level* was recoded as: people without basic studies and people with primary school or higher. These two levels established significant difference between survivor curves.

The results obtained in the multivariate analysis performed with the Cox proportional hazards regression model are shown in the Table 3. Multivariate Cox models for predict dependence and frailty included the same three variables coded as: *gender* (male, female), *marital status* (with partner, no partner) and *chronicity level* (healthy person or with a low complexity chronic disease, medium or severe complexity chronic disease). Results of both models establish that a female with partner and with a moderate or severe chronic disease is the worst prognosis of dependence and frailty. In the case of the multivariate Cox model for survival time, the variables included in this model were coded as: *gender* (male, female), *educational level* (no basic studies, primary school or higher) and Frail-VIG index (No frail, Frail). In that case, the worst prognosis in the survival experience for a patient with 70 years old is to be male, without basic studies and with a classification of frail person using de VIG index.

Figure 4 shows the nomograms for deriving estimates of dependence and frailty and Figure 5 for deriving estimates of overall survival. To read nomogram, a vertical

Table 2. Mean age ± error standard of time free of dependence, time free of frailty and survival time. P-value of equality of survivor curves contrasted with the Log-Rank test.

	Dependence-free Time		Frailty-free Time		Survival Time	
	Mean Age (E.S.)	p-value	Mean Age (E.S.)	p-value	Mean Age (E.S.)	p-value
Gender						
Male	87.09 (1.03)	0.468	86.05 (1.01)	0.784	91.44 (1.20)	0.004
Female	86.07 (0.50)		85.86 (0.55)		92.88 (0.80)	
Marital state						
With partner	84.25 (0.60)	<0.001	83.27 (0.56)	<0.001	89.20 (0.66)	0.008
No partner	87.83 (0.55)		87.61 (0.64)		93.85 (0.77)	
Educational level						
No Read/Write	85.53 (0.90)		84.85 (0.99)		88.59 (0.97)	
Primary studies	86.53 (0.54)	0.457	86.48 (0.59)	0.057	93.77 (0.75)	0.008
High school or higher	84.22 (1.16)		82.24 (1.09)		86.81 (0.72)	
Number cohabitants						
Live alone	87.71 (0.80)		87.51 (0.84)		89.83 (0.77)	
2 cohabitants	84.44 (0.78)	0.052	84.67 (0.74)	0.033	89.10 (1.08)	0.448
3 or more cohabitants	86.93 (0.46)		85.99 (0.83)		89.15 (0.89)	
Chronicity level						
Healthy/Low level	89.65 (0.85)		90.92 (0.86)		95.38 (1.00)	
Medium level	85.21 (0.65)	<0.001	84.44 (0.67)	<0.001	92.53 (1.09)	<0.001
Severe level	84.34 (0.46)		83.04 (0.81)		88.94 (1.00)	
Barthel index						
No dependent					93.80 (0.89)	0.047
Dependent					91.87 (0.68)	
SPPB index						
No frail	87.57 (0.83)	0.588			90.66 (0.55)	0.411
Frail	86.37 (0.58)				93.94 (0.79)	
Frail-VIG index						
No frail	88.44 (0.93)	0.001			96.45 (0.73)	<0.001
Frail	85.20 (0.57)				90.95 (0.82)	

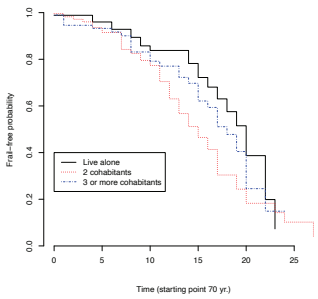


(a) Marital estate (p value <0.001).

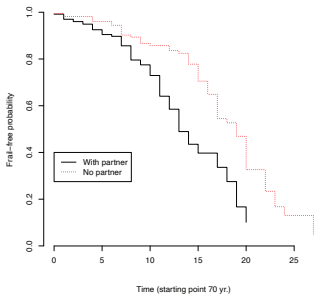
(b) Chronicity disease level (p value <0.001).

(c) Frail-VIG (p value 0.001).

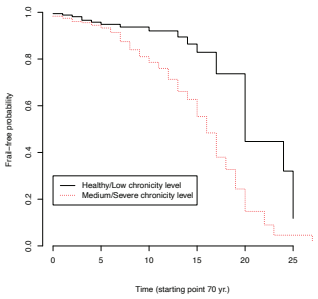
Figure 1. Kaplan-Meier estimates of the Dependence-free functions.



(a) Number cohabitants (p value 0.033).

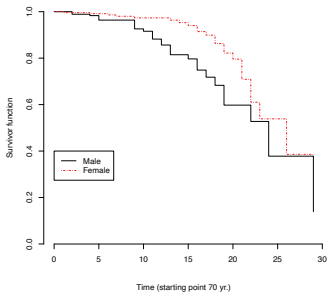


(b) Marital state (p value <0.001).

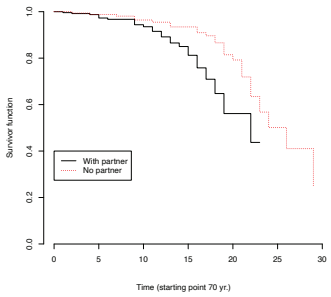


(c) Chronicity disease level (p value <0.001).

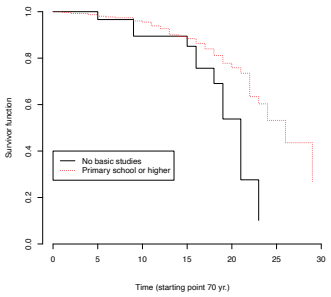
Figure 2. Kaplan-Meier estimates of the Frailty-free functions.



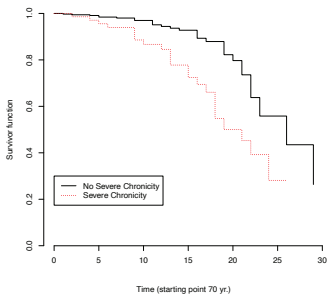
(a) Gender (p value 0.004).



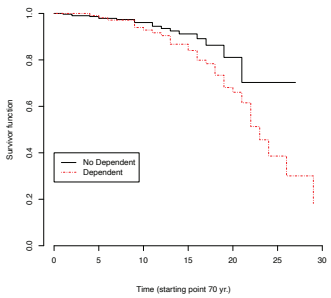
(b) Marital state (p value 0.008).



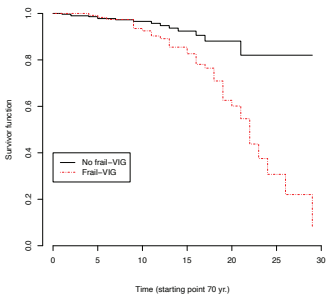
(c) Educational level (p value 0.003).



(d) Chronicity level (p value <0.001).



(e) Barthel index (p value 0.047).

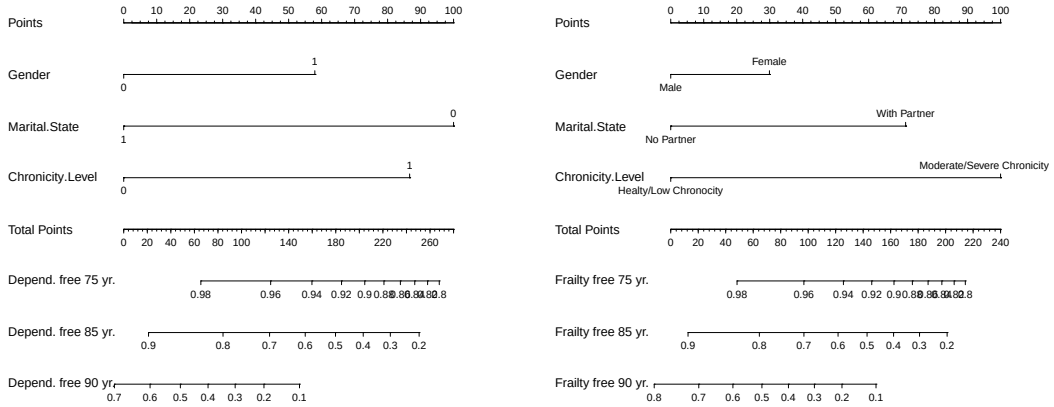


(f) Frail-VIG index (p value <0.001).

Figure 3. Kaplan-Meier estimates of the survivor functions.

Table 3. Multivariate Cox models analysis of time to dependence, frailty and survival.

Covariate	$\hat{\beta}$	e.s.($\hat{\beta}$)	z	*p-value*	exp($\hat{\beta}$)	I.C$_{95\%}$ exp($\hat{\beta}$) Inf.	Sup.
			Dependence				
Gender	0.688	0.228	3.018	0.002	1.99	1.27	3.11
Marital status	-1.187	0.238	-4.993	<0.001	0.31	0.19	0.49
Chronicity level	1.029	0.240	4.252	<0.001	2.80	1.74	4.50
			Frailty				
Gender	0.468	0.209	2.230	0.026	1.60	1.06	2.41
Marital status	-1.088	0.223	-4.882	<0.001	0.33	0.22	0.52
Chronicity level	1.512	0.271	5.573	<0.001	4.53	2.66	7.71
			Survival				
Gender	-0.968	0.281	-3.451	0.001	0.38	0.22	0.66
Educational level	-0.811	0.348	-2.329	0.020	0.45	0.23	0.88
Frail-VIG	1.070	0.319	3.346	0.001	2.92	1.56	5.46



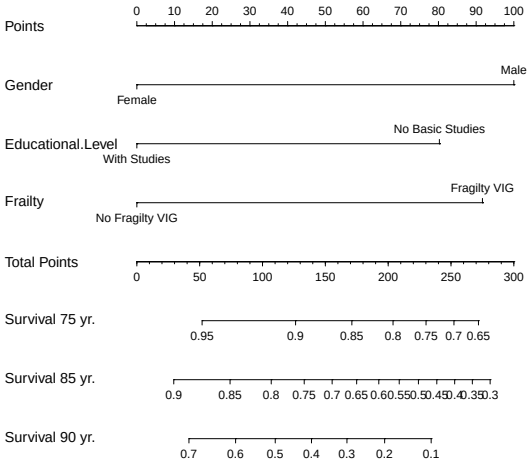
(a) Dependence. (b) Frailty.

Figure 4. Nomograms for predicting Dependence-free and Frailty-free at 75, 85 and 90 years old.

line must be drawn from each tick mark indicating the characteristics of the patient to the top axis (*Points*). Once the total points with all the characteristics have been computed, the corresponding number must be found on the axis (*Total Points*). Then, from this localized value of total points drawing a vertical line down to the probability axis, the probabilities of being event-free at 75, 85 and 90 years old are obtained. To assess model accuracy (discriminatory ability), the concordance index c was calculated, obtained a value of $c = 0.69$ for dependence model, $c = 0.70$ for frailty model and $c = 0.66$ for survival model.

4. Discussion

In our research we studied the sociodemographic and clinical risk factors in general population aged 70 years or over that may influence in frailty, dependency and mortality. Then, we developed mathematical models and nomograms to predict these adverse



(a) Survival.

Figure 5. Nomograms for predicting survival at 75, 85 and 90 years old.

outcomes. The prognosis factors estimated are variables easy to obtain in the medical assistance except the chronicity level, shown usually by the computerized medical history shows it.

To the best of our knowledge, there are few studies in occidental population that develop mathematical models and nomograms of frailty, dependency and mortality. This is the first made in Spanish population, in an average income population. We studied previously in this sample the clinical risk factors of frailty and dependency and developed mathematical models [11]. Currently we study mortality at three years in the same sample, in order to analyze the risk factors related to frailty, dependency and mortality.

In previous mathematical models considering frailty, they use the Fried's criteria [16, 17, 19] or a frailty index developed just for that study. In our study we use frail-VIG index, already used in various investigations [5, 10, 54, 56]. This is a difference between previous mortality models [13, 40, 51] that use diverse frailty indexes: in each one of them, they developed a different frailty index based on the Searle's methodology [45]. The rules of this methodology are the following: at first, variables might to be selected by the following criteria: variables must be deficits associated with health status; a deficit's prevalence must be generally increased with age, although some clearly age-related adverse conditions can decrease in prevalence at very advanced ages due to survivor effects; the chosen deficits must not be saturated too early; when considering the candidate deficits as a group, the deficits that make up a frailty index must cover a range of systems; and if a single frailty index is to be used serially on the same people, the items that make up the frailty index need to be the same from one iteration to the next. Deficits should be added until 30-40 deficits, but 20 is the minimum required [12].

The results of the multivariate Cox models determine that the risk factors for developing frailty or dependency are female gender, chronicity level 2 or 3, and marriage. The risk factors for mortality are male gender, low educational level and being frail

according to frail-VIG index. We can equate in our study the hierarchy described by Zamudio et al [58] of the continuum between physical frailty and dependency, but using the frail-VIG index. Time free of dependency is higher in each group than time free of frailty in the predictive models.

About risk factors, we observed that frail people have a risk of dying almost three times higher than a patient classified as not frail. Frailty, measured with Fried's criteria or with a frail index, increases with age [19, 48], and each of them has modest but comparable ability to predict all-cause of mortality [31]. Recently, Stolz et al concluded that the rate of the frail index change is more important than the current frail index level for short-term mortality prediction among the oldest old [51]. This differs from Bai et al [6] results (cohort studied for 40 years), study in which the current level of the frail index is as a stronger marker for risk stratification than the rate of change. Frailty is related with disability and morbidity: they are associated with each other and may overlap [19, 44, 53]. Between 23% and 26% of the frail elderly people do not have disability or comorbidity [2], but we see that comorbidity is a clinical risk factor for frailty, dependency and mortality. In our research, chronicity level was a risk factor in the univariate analysis of frailty, dependence and mortality, but not in the multivariate analysis of mortality. The frail-VIG index includes various diseases variables, but chronicity level was not significant in the mortality model. This topic could be the subject of future studies: analyzing which variable best predicts mortality, chronicity level or frailty.

Gender influences on the three adverse outcomes, but in a different way. Dependence and frailty risk is higher in women than men, but mortality risk is lower in case of women. In the multivariate analysis we obtained a 62% mortality reduction in women compared with men. This finding is aligned with the Zhang et al [59] study, in which women had higher frailty than men, but men higher mortality than women. In a recent meta-analysis is described as a no association between gender and frailty-mortality's [18]. There is controversy on this topic regarding gender and frailty-mortality's association, and future studies should investigate this association. Regarding marital status, be married was a risk factor for frailty, dependency and mortality. It differs of other studies that analyzed this topic: a meta-analysis of cross-sectional data regarding associations between marital status and frailty among community-dwelling older people showed almost twice higher frailty risk in unmarried individuals compared with married individuals [32]. One possible explanation is that psychological stress and social isolation are related with singles, and this increases unhealthy behaviours [32]. Trevisan et al [55] found differences between gender, marital status and frailty: single men had higher risk of frailty, and widowed women showed less risk than married ones. The greater risk of frailty and dependency in married people could have two explanations. At first, married people could fulfill the needs between them. In second place, many people unable to be independent go to a nursing home, they are institutionalized.

Although SPPB is a disability indicator [26] and an important tool for decision-making in frailty management algorithms [37], in our study SPPB was not a prognosis factor for frailty, dependency or mortality. We used the cut-off point "7", because it was the best one identified in the Fradea's study [1] to associate frailty, and this cut-off point increases the risk of mortality [15]. The absence of the relationship could have two explanations: first, several participants could not take the SPPB because they did not understand the instructions and process, or they physically could not do it at all (there were robust patients who had been operated); second, there could be a fast deterioration in the SPPB level over the three years.

Finally, low educational level increases the mortality risk. This association has also

been observed in the Stolz et al study [51], and in the HRS, ELSA, LASA and SHARE cohorts [7, 30, 49, 50].

Nomograms are a visual and easy tools to use in a clinic context. Most of the nomograms related to frailty in community dwelling have been recently developed in the eastern population. In 2021 Bing-Ru et al [17] developed a nomogram to predict the frailty progression (measured with Fried's criteria) in people aged 60 years or over the in general population. In 2022, Li et al [33] developed a nomogram with 30 variables to predict frailty using a frailty index in Chinese people. We consider that Li's nomogram could not be applicable in other countries due to proposed variables: in addition to age, physical exercise... there is the weekly consumption of garlic or being Han race. Gu et al [24] developed in 2022 a prediction model to estimate mortality in the oldest old, and consider too the Han race. Both models would require adaptation for the application in other countries.

Respect dependency nomograms, a systematic review published in 2022 [23] concluded that no model for functional status can be recommended for implementation in practice. Recently, Gobbens et al [21] developed nomograms to predict total disability, activities of daily living disability (ADL) and instrumental activities of daily living disability (IADL), using the Tilburg Frailty Indicator (TFI) [21]. The variables of the nomogram were the TFI items, they do not take into account disease's related variables. The three nomograms developed in our study are composed of variables easily obtainable by the physician, only the chronicity level must be given by the computerized medical history. It is easy to calculate time free from frailty, dependency and mortality using them.

One strength of the study is that it was carried out in the general population in an average income population. All patients 70 years or older from two physicians were included except those institutionalized. The internal validity and the concordance index for the three models are adequate (c=0.70 for the frailty model, c=0,69 for the dependence model and c=0,66 for the survival model).

Several limitations of this study should be addressed. The external validity is limited because the sample is a small group in one specific geographical area. There are few patients with advanced frailty because institutionalized people were excluded. It was very difficult to collect their data, but we collected the data from patients bedridden at home. External validity will be performed in the future with new data.

We selected the age of 70 years because it is when the Spanish Ministry of Health [37] recommends screening for frailty. In our study we can see important differences between diverse groups, for example: the probability at 85 years old to be free of dependency of a non-married men with low chronicity level is 99.2%, and 17.3% for a married woman with moderate or high chronicity. Our results can help healthcare professionals to empower patients by calculating their risks of frailty, dependency and mortality. The competent authorities could consider the risks obtained to design a health plan for the elderly.

5. Conclusions

In conclusion, we developed three models and nomograms to estimate the frailty, dependency and mortality risk for 70-years-old in general population, and analyzed the risk factors. The health actions to prevent frailty and dependence should focus on reducing the chronicity level, especially in women. To delay mortality, an individualized approach should be implemented in frail people. The risks are easy to calculate by the

doctor with the nomograms, and differences observed between the groups of models imply the adaptation of the clinical needs of the patients. Further studies are needed to determine other health and social risk factors, also analyzing the differences between genders.

References

[1] P. Abizanda, L. Romero, P. Sánchez-Jurado, P. Atienzar-Núñez, J. Esquinas-Requena, and I. Garcia-Nogueras, *Association between functional assessment instruments and frailty in older adults: The fradea study*, Journal of Frailty & Aging (2012), pp. 1–7.

[2] M.V.C. Alcalá, Á.O. Puime, M.T.S. Santos, A.G. Barral, J.I.G. Montalvo, and M.V. Zunzunegui, *Prevalencia de fragilidad en una población urbana de mayores de 65 años y su relación con comorbilidad y discapacidad*, Atención Primaria 42 (2010), pp. 520–527.

[3] J. Amblàs-Novellas, J.C. Martori, N.M. Brunet, R. Oller, X. Gómez-Batiste, and J.E. Panicot, *Índice frágil-VIG: diseño y evaluación de un índice de fragilidad basado en la valoración integral geriátrica*, Revista Española de Geriatría y Gerontología 52 (2017), pp. 119–127.

[4] J. Amblàs-Novellas, J.C. Martori, J. Espaulella, R. Oller, N.M. Brunet, M. Inzitari, and R. Romero-Ortuno, *Frail-vig index: a concise frailty evaluation tool for rapid geriatric assessment*, BMC Geriatrics 18 (2018), pp. 1471–2318.

[5] G. Badosa-Collell, N. Latorre-Vallbona, J.C. Martori, R. Oller, J.C. Trullàs, and J. Amblàs-Novellas, *Capacidad predictiva de mortalidad del índice frágil-vig (if-vig) en pacientes ancianos con fractura de fémur*, Revista Española de Geriatría y Gerontología 57 (2022), pp. 220–223.

[6] G. Bai, A. Szwajda, Y. Wang, X. Li, H. Bower, I.K. Karlsson, B. Johansson, A.K.D. Aslan, N.L. Pedersen, S. Hägg, and J. Jylhävä, *Frailty trajectories in three longitudinal studies of aging: Is the level or the rate of change more predictive of mortality?*, Age and Ageing 50 (2021), pp. 2174–2182.

[7] A. Börsch-Supan, M. Brandt, C. Hunkler, T. Kneip, J. Korbmacher, F. Malter, B. Schaan, S. Stuck, and S. Zuber, *Data resource profile: The survey of health, ageing and retirement in europe (SHARE)*, International Journal of Epidemiology 42 (2013), pp. 992–1001.

[8] K. Bouillon, M. Kivimaki, M. Hamer, S. Sabia, E.L. Fransson, A. Singh-Manouxand, C.R. Gale, and G.D. Batty, *Measures of frailty in population-based studies: an overview.*, BMC Geriatr. 13 (2013). Available at http://www.biomedcentral.com/1471-2318/13/64%0ARESEARCH.

[9] Á. Caballero-Mora, *Knowing Frailty at Individual Level: A Systematic Review WP Leader: UCSC Work package: WP4* (2017).

[10] S. Camacho-Torregrosa, X. Albert-Ros, J. Aznar-Cardona, M. Mollar-Talamantes, M.A. Bordonaba-Mateos, and J.V. Galán-Bernardino, *Índice frágil-vig: Validez convergente y discriminativa respecto a la short physical performance battery en población general*, Revista Española de Geriatría y Gerontología 58 (2023), pp. 75–83.

[11] S. Camacho Torregrosa, C. Santamaría Navarro, and X. Albert Ros, *Mathematical modelling of frailty and dependency in basic activities of daily living in general population aged 70 years.*, Modelling for engineering and Human behaviour 2022. Proceedings (2022), pp. 41–46.

[12] M. Cesari, *There is much more than just diseases that underlies frailty in older persons*, Aging clinical and experimental research 31 (2019), pp. 1349–1350.

[13] Q. Chen, B. Tang, Y. Zhai, Y. Chen, Z. Jin, H. Han, Y. Gao, C. Wu, T. Chen, and J. He, *Dynamic statistical model for predicting the risk of death among older chinese people, using longitudinal repeated measures of the frailty index: a prospective cohort study*, Age and Ageing 49 (2020), pp. 966–973.

[14] D. Collett, *Modelling Survival Data in Medical Research*, segunda ed., Chapman-

Hall/CRC, 2003.

[15] C. de Fátima Ribeiro Silva, D.G. Ohara, A.P. Matos, A.C.P.N. Pinto, and M.S. Pegorari, *Short physical performance battery as a measure of physical performance and mortality predictor in older adults: A comprehensive literature review*, International Journal of Environmental Research and Public Health 18 (2021), p. 10612.

[16] J.A.V. de Sousa, M.H. Lenardt, C.R.B. Grden, L. Kusomota, M.S.G. Dellaroza, and S.E. Betiolli, *Physical frailty prediction model for the oldest old*, Revista Latino-Americana de Enfermagem 26 (2018).

[17] B.R. Dong, X.Q. Gu, H.Y. Chen, J. Gu, and Z.G. Pan, *Development and validation of a nomogram to predict frailty progression in nonfrail chinese community-living older adults*, Journal of the American Medical Directors Association 22 (2021), pp. 2571–2578.e4.

[18] Y. Fan, J. Huang, Y. Zhou, X. Gu, and D. Gong, *Does the impact of frailty on all-cause mortality in older persons differ between women and men? a meta-analysis*, Journal of the American Medical Directors Association 22 (2021), pp. 606.e1–606.e6.

[19] L.P. Fried, C.M. Tangen, J. Walston, A.B. Newman, C. Hirsch, J. Gottdiener, T. Seeman, R. Tracy, W.J. Kop, G. Burke, and M.A. McBurnie, *Frailty in older adults: Evidence for a phenotype*, The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 56 (2001), pp. M146–M157.

[20] V. Gaigbe-Togbe, L. Bassarsky, D. Gu, T. Spoorenberg, and L. Zeifman, *World population prospects 2022*, https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/.

[21] R.J. Gobbens, L.M. Santiago, I. Uchmanowicz, and T. van der Ploeg, *Predicting Disability Using a Nomogram of the Tilburg Frailty Indicator (TFI)*, in *Healthcare*, Vol. 11. MDPI, 2023, p. 1150.

[22] R.J. Gobbens, K.G. Luijkx, M.T. Wijnen-Sponselee, and J.M. Schols, *In search of an integral conceptual definition of frailty: opinions of experts*, Journal of the American Medical Directors Association 11 (2010), pp. 338–343.

[23] B.V. Grootven and T. van Achterberg, *Prediction models for functional status in community dwelling older adults: a systematic review*, BMC Geriatrics 22 (2022).

[24] Y. Gu, W. Wu, C. Kong, Q. Luo, L. Ran, X. Tan, and Q. Zhang, *Development of prognostic prediction model to estimate mortality for frail oldest old: prospective cohort study*, The Journals of Gerontology: Series A 78 (2023), pp. 711–717.

[25] J.M. Guralnik, E.M. Simonsick, L. Ferrucci, R.J. Glynn, L.F. Berkman, D.G. Blazer, P.A. Scherr, and R.B. Wallace, *A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission*, Journal of Gerontology 49 (1994), pp. M85–M94.

[26] J.M. Guralnik, L. Ferrucci, E.M. Simonsick, M.E. Salive, and R.B. Wallace, *Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability*, New England Journal of Medicine 332 (1995), pp. 556–562.

[27] S.E. Hardy and T.M. Gill, *Recovery from disability among community-dwelling older persons*, Jama 291 (2004), pp. 1596–1602.

[28] J. Harrell Frank E., R.M. Califf, D.B. Pryor, K.L. Lee, and R.A. Rosati, *Evaluating the Yield of Medical Tests*, JAMA 247 (1982), pp. 2543–2546.

[29] F.E. Harrell Jr, *rms: Regression Modeling Strategies* (2019). Available at https://CRAN.R-project.org/package=rms, R package version 5.1-3.1.

[30] E.O. Hoogendijk, D.J.H. Deeg, S. de Breij, S.S. Klokgieters, A.A.L. Kok, N. Stringa, E.J. Timmermans, N.M. van Schoor, E.M. van Zutphen, M. van der Horst, J. Poppelaars, P. Malhoe, and M. Huisman, *The longitudinal aging study amsterdam: cohort update 2019 and additional data collections*, European Journal of Epidemiology 35 (2019), pp. 61–74.

[31] D.J. Kim, M.S. Massa, C.M. Potter, R. Clarke, and D.A. Bennett, *Systematic review of the utility of the frailty index and frailty phenotype to predict all-cause mortality in older people*, Systematic Reviews 11 (2022).

[32] G. Kojima, K. Walters, S. Iliffe, Y. Taniguchi, and N. Tamiya, *Marital status and risk of physical frailty: A systematic review and meta-analysis*, Journal of

the American Medical Directors Association 21 (2020), pp. 322–330. Available at https://doi.org/10.1016/j.jamda.2019.09.017.

[33] S. Li, W. Fan, B. Zhu, C. Ma, X. Tan, and Y. Gu, *Frailty risk prediction model among older adults: a chinese nation-wide cross-sectional study*, International Journal of Environmental Research and Public Health 19 (2022), p. 8410.

[34] M. López-Ratón, M.X. Rodríguez-Álvarez, C.C. Suárez, and F.G. Sampedro, *OptimalCutpoints: An R package for selecting optimal cutpoints in diagnostic tests*, Journal of Statistical Software 61 (2014), pp. 1–36. Available at http://www.jstatsoft.org/v61/i08/.

[35] J.L. Lund, T.M. Kuo, M.A. Brookhart, A.M. Meyer, A.F. Dalton, C.E. Kistler, S.B. Wheeler, and C.L. Lewis, *Development and validation of a 5-year mortality prediction model using regularized regression and medicare data*, Pharmacoepidemiology and drug safety 28 (2019), pp. 584–592.

[36] L. Menéndez-González, A. Izaguirre-Riesgo, S. Tranche-Iparraguirre, Á. Montero-Rodríguez, and M.I. Orts-Cortés, *Prevalencia y factores asociados de fragilidad en adultos mayores de 70 años en la comunidad*, Atención Primaria 53 (2021), p. 102128.

[37] Ministerio de Sanidad, *Actualización del documento de consenso sobre prevención de la fragilidad en la persona mayor* (2022). Informes, estudios e investigación.

[38] M. Moreno-Arino, I. Torrente Jimenez, A. Cartanya Gutierrez, J.C. Oliva Morera, and R. Comet, *Assessing the strengths and weaknesses of the clinical frailty scale through correlation with a frailty index*, Aging Clinical and Experimental Research 32 (2020), pp. 2225–2232.

[39] Y. Peng, G.C. Zhong, X. Zhou, L. Guan, and L. Zhou, *Frailty and risks of all-cause and cause-specific death in community-dwelling adults: a systematic review and meta-analysis.*, BMC Geriatr 22 (2022), p. 725. Available at https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-022-03404-w.

[40] A.A. Pereira, F.S.A. Borim, I. Aprahamian, and A.L. Neri, *Comparison of two models of frailty for the prediction of mortality in brazilian community-dwelling older adults: The FIBRA study*, The journal of nutrition, health & aging 23 (2019), pp. 1004–1010.

[41] F. Rivas-Ruiz, M. Machón, E. Contreras-Fernández, K. Vrotsou, M. Padilla-Ruiz, A.I. Diez Ruiz, Y. de Mesa Berenguer, I. Vergara, and G. GIFEA, *Prevalence of frailty among community-dwelling elderly persons in spain and factors associated with it*, European Journal of General Practice 25 (2019), pp. 190–196.

[42] L.R. Rizos and P.A. Soler, *Fragilidad como predictor de episodios adversos en estudios epidemiológicos: revisión de la literatura*, Revista Española de Geriatría y Gerontología 48 (2013), pp. 285–289.

[43] K. Rockwood, *A global clinical measure of fitness and frailty in elderly people*, Canadian Medical Association Journal 173 (2005), pp. 489–495.

[44] A. Rodríguez-Laso, M. Caballero Mora, I. García Sánchez, C. Alonso Bouzón, L. Rodríguez Mañas, R. Bernabei, B. Gabrovec, A. Hendry, A. Liew, R. O'Caoimh, *et al.*, *Updated state of the art report on the prevention and management of frailty*, European Union (2019).

[45] S.D. Searle, A. Mitnitski, E.A. Gahbauer, T.M. Gill, and K. Rockwood, *A standard procedure for creating a frailty index*, BMC Geriatrics 8 (2008).

[46] S. Setiati, P.W. Laksmi, I. Aryana, S. Sunarti, N. Widajanti, L. Dwipa, E. Seto, R. Istanti, L.J. Ardian, and S.C. Chotimah, *Frailty state among indonesian elderly: prevalence, associated factors, and frailty state transition*, BMC geriatrics 19 (2019), pp. 1–10.

[47] S. Shah, F. Vanclay, and B. Cooper, *Improving the sensitivity of the barthel index for stroke rehabilitation*, Journal of Clinical Epidemiology 42 (1989), pp. 703–709.

[48] X. Song, A. Mitnitski, and K. Rockwood, *Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation*, Journal of the American Geriatrics Society 58 (2010), pp. 681–687.

[49] A. Sonnega, J.D. Faul, M.B. Ofstedal, K.M. Langa, J.W. Phillips, and D.R. Weir, *Cohort profile: the health and retirement study (HRS)*, International Journal of Epidemiology 43 (2014), pp. 576–585.

[50] A. Steptoe, E. Breeze, J. Banks, and J. Nazroo, *Cohort profile: The english longitudinal study of ageing*, International Journal of Epidemiology 42 (2012), pp. 1640–1648.
[51] E. Stolz, H. Mayerl, and E.O. Hoogendijk, *Frailty in the oldest old: is the current level or the rate of change more predictive of mortality?*, Age and Ageing 51 (2022).
[52] R.D.C. Team, *R: A Language and Environment for Statistical Computing*, R Foundation for Statistical Computing, Vienna, Austria (2010). http://www.R-project.org.
[53] O. Theou, M.R. Rockwood, A. Mitnitski, and K. Rockwood, *Disability and co-morbidity in relation to frailty: how much do they overlap?*, Archives of gerontology and geriatrics 55 (2012), pp. e1–e8.
[54] A. Torné, E. Puigoriol, E.Z. del Olmo, J.J. Zamora-Sánchez, S. Santaeugènia, and J. Amblàs-Novellas, *Reliability, validity, and feasibility of the frail-VIG index*, International Journal of Environmental Research and Public Health 18 (2021), p. 5187.
[55] C. Trevisan, N. Veronese, S. Maggi, G. Baggio, M.D. Rui, F. Bolzetta, S. Zambon, L. Sartori, E. Perissinotto, G. Crepaldi, E. Manzato, and G. Sergi, *Marital status and frailty in older people: Gender differences in the progetto veneto anziani longitudinal study*, Journal of Women's Health 25 (2016), pp. 630–637.
[56] J.J. Zamora-Sánchez, E. Zabaleta-del Olmo, V. Gea-Caballero, I. Julián-Rochina, G. Pérez-Tortajada, and J. Amblàs-Novellas, *Convergent and discriminative validity of the frail-vig index with the eq-5d-3l in people cared for in primary health care*, BMC geriatrics 21 (2021), pp. 1–7.
[57] J.J. Zamora-Sánchez, E. Zabaleta-del Olmo, V. Gea-Caballero, I. Julián-Rochina, G. Pérez-Tortajada, and J. Amblàs-Novellas, *Validez convergente y discriminativa del índice frágil-vig con la escala de braden en personas atendidas en atención domiciliaria*, Revista Española de Geriatría y Gerontología 57 (2022), pp. 71–78.
[58] A. Zamudio-Rodríguez, L. Letenneur, C. Féart, J.A. Avila-Funes, H. Amieva, and K. Pérès, *The disability process: is there a place for frailty?*, Age and Ageing 49 (2020), pp. 764–770.
[59] Q. Zhang, H. Guo, H. Gu, and X. Zhao, *Gender-associated factors for frailty and their impact on hospitalization and mortality among community-dwelling older adults: a cross-sectional population-based study*, PeerJ 6 (2018), p. e4326.

Appendix A. Frail-VIG index

Frail-VIG index					
Domain		**Variable**	**Description**	**Yes**	**No**
Functional	IADLs	Money management	Needs help managing financial matters (bank, shops, restaurants)	1	0
		Telephone use	Needs help using the telephone	1	0
		Medication management	Needs assistance in preparing or administering medications	1	0
	BADLs	Barthel Index (BI)	No dependency (IB ≥ 95)	0	
			Mild-moderate dependency (IB 90-65)	1	
			Moderate-severe dependency (IB 60-25)	2	
			Absolute dependency (IB ≤20)	3	
Nutritional		Malnutrition	Weigh loss ≥ 5% in the last 6 months	1	0
Cognitive		Degree of cognitive impairment	No cognitive impairment	0	
			Mild-moderate cognitive impairment (equivalent to GDS ≤5)?	1	
			Severe-very severe cognitive impairment (equivalent to GDS ≥ 6)?	2	
Emotional		Depressive syndrome	Need for antidepressant medication	1	0
		Insomnia/anxiety	Frequent need for benzodiazepines or other psychiatric drugs with a sedative effect for insomnia/anxiety	1	0
Social		Social vulnerability	Do health care professionals perceive the presence of social vulnerability?	1	0
Geriatric syndromes		Delirium	Presence of delirium and/or behaviour disorder requiring antipsychotic drugs in the last 6 months	1	0
		Falls	In the last 6 months, ≥2 falls or hospitalization due to a fall	1	0
		Ulcers	Presence of ulcer (pressure or vascular, any grade)	1	0
		Polypharmacy	Taking ≥ 5 drugs	1	0
		Dysphagia	Difficulty swallowing when eating or drinking? Presence of aspiration respiratory infections during the last 6 months?	1	0
Severe symptoms		Pain	Need for ≥2 conventional analgesics and/or strong opioids for pain control	1	0
		Dyspnea	Basal dyspnea impeding the ability to leave the house and/or opioids are frequently needed	1	0
Diseases (+)		Cancer	Active cancer	1	0
		Respiratory	Presence of any type of chronic respiratory disease	1	0
		Cardiac	Presence of any type of chronic heart disease	1	0
		Neurological	Presence of any type of neurodegenerative disease or a history of stroke	1	0
		Digestive	Presence of any type of chronic digestive disease	1	0
		Renal	Presence of chronic renal failure (Glomerular filtration rate <60)	1	0
Frail-VIG index (X/25)					
ADLs Basic Activities of Daily Living, IAVDs Instrumental Activities of Daily Living, GDS Global Deterioration Scale. (+) two point are scored if the patient presents criteria for advanced chronic illness on the NECPAL test, available at: http://ico.gencat.cat/web/.content/minisite/ico/professionals/documents/qualy/arxius/NECPAL-3.0-ENGLISH_full-version.pdf					