Predictors of Frailty and Vitality in Older Adults Aged 75 years and Over: Results from the Longitudinal Aging Study Amsterdam

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Keywords

Frailty · Vitality · Prediction models · Longitudinal Aging Study Amsterdam

Abstract

Introduction: Frailty can be seen as a continuum, from fit to frail. While many recent studies have focused on frailty, much less attention has been paid to the other end of the continuum: the group of older adults that remain (relatively) vital. Moreover, there is a lack of studies on frailty and vitality that investigate predictors from multiple domains of functioning simultaneously. The aim of this study was to identify predictors of frailty as well as vitality among older adults aged 75 years and over. **Methods:** We used longitudinal data from 569 adults aged ≥ 75 years who participated in the Longitudinal Aging Study Amsterdam. Predictors from the sociodemographic, social, psychological, lifestyle, and physical domains of functioning were measured at T1 (2008–2009). We used the frailty index (FI) to identify frail ($FI \geq 0.25$) and vital ($FI \leq 0.15$) respondents at follow-up, 3 years later (T2: 2011–2012). We conducted logistic regression analyses with backward stepwise selection to develop and internally validate our prediction models. **Results:** The prevalence of frailty in our sample at follow-up was 49.4% and the prevalence of vitality was 18.3%. Predictors of frailty and vitality partly overlapped and included age, depressive symptoms, number of chronic diseases, and self-rated health. We also found predictors that did not overlap. Male sex, moderate alcohol use, more emotional support received, and no hearing problems, were predictors of vitality. Lower cognitive functioning, polypharmacy, and pain were predictors of frailty. The final model for vitality explained 42% of the variance and the final model for frailty explained 48%. Both models had a good discriminative value (area under ROC-curve [AUC] vitality: 0.88; AUC frailty: 0.85). **Conclusion:** Among older adults aged 75 years and over, predictors of frailty only partially overlap with predictors of vitality. The readily accessible predictors in our models may help to identify older adults who are likely to be vital, or who are at risk of frailty.

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Published by S. Karger AG, Basel

Introduction

In the coming years, the proportion of older adults in the population will increase dramatically. In the Netherlands, the number of people aged 75 years and over will more than double by 2040 [1]. Although advanced age is

not synonymous with frailty, the incidence of frailty does increase with age. Therefore, a sharp increase in the prevalence of frailty is expected [2].

Frailty does not yet have a standard definition [3], but a widely used definition is that frailty is a state of vulnerability to poor resolution of homeostasis after a stressor event due to an accelerated decrease in physiological reserve [4]. Frailty can be seen as a continuum, from fit (i.e., vital) to frail [5, 6]. While most research has focused on older adults becoming frail, there is also a group of older adults who remain (relatively) vital [6–8].

Many studies have attempted to identify risk factors of frailty. In the sociodemographic domain, sex, educational level, income, and marital status have been shown to be associated with frailty. Studies examining the social domain have found loneliness and the level of social participation to be associated with frailty. With regard to the psychological domain, control beliefs, depressive symptoms, and cognitive impairment were found to be associated with frailty. In the physical domain, associations have been found between BMI, (number of) chronic diseases, polypharmacy, hypertension, sensory problems, pain, and frailty. And last, in the lifestyle domain, physical activity, smoking, alcohol use, and sleep have been found to be associated with frailty [2, 9].

However, most of these studies included risk factors from 1 or 2 domains of functioning only and built association models, not prediction models. Therefore, it is not yet clear how these factors interact and which set of factors actually predict frailty. To our knowledge, only 1 study tried to develop and validate a prediction model including multi-domain risk factors [10]. Ng et al. [10] found that, in their sample of older adults aged 55 and over in Singapore, almost all of their 40 candidate predictors were univariably associated with frailty or pre-frailty. However, in their final model, only older age, having no education, heart failure, obstructive respiratory disorders, stroke, depressive symptoms, hearing impairment, visual impairment, chronic airflow obstruction, chronic kidney failure, low hemoglobin, high nutritional risk, and inflammation markers predicted frailty [10]. However, these results cannot necessarily be generalized to other countries and other age-groups. No such studies have been conducted in Europe or in an older population.

Research on vitality in older adults is scarce. When examining frailty as a continuum, the absence of deficits in multiple domains can be considered as vitality. Vitality has been identified as an important domain of “intrinsic capacity” or successful aging [11], but it is not yet clear which factors are associated with or predict vitality in old-

er adults. A study examining transitions in vitality status in Italian older adults aged 65 years and over found educational level, age, sex, BMI, and depressive symptoms to be associated with vitality status [8]. More research is needed to identify a set of predictors of vitality in older adults. The frailty index (FI) is an often-used instrument to measure frailty, and it is based on the accumulation of deficits [7]. And while it has mostly been used to measure (gradations in) frailty, the FI is a sensitive measure and it encompasses the entire continuum, from fit to frail [12]. In the current study, we will, therefore, use the FI as a measure of frailty as well as vitality.

Older people with frailty are at increased risk of adverse outcomes such as hospitalization, disability, and mortality [2, 4, 13]. Previous studies have shown that the risk of certain adverse outcomes due to frailty, for example, hospitalization [13] and falls [14], was highest among older adults aged 75 years and over, an age-group that will grow rapidly in the coming years [1]. Therefore, special attention should be paid to this specific age-group.

Knowledge of the predictors of frailty is essential for early identification of at-risk individuals. Furthermore, identifying a set of predictors of frailty and vitality may help the development of strategies to prevent or delay the onset of frailty while identifying predictors of vitality may help to promote vitality among older adults. Therefore, the aim of this study was to identify predictors of frailty and vitality among older adults aged 75 years and over.

Materials and Methods

Sample

We used data from the Longitudinal Aging Study Amsterdam (LASA). LASA is an ongoing, prospective cohort study in the Netherlands on the determinants, trajectories, and consequences of physical, cognitive, emotional, and social functioning in older adults aged 55 years or older. Measurements are conducted approximately every 3 years and include a main face-to-face computer-assisted interview, a face-to-face computer-assisted medical interview in which clinical measurements are performed and additional questions are asked, and a self-administered questionnaire. A telephone interview is offered to those respondents who refused to participate in a full or an abbreviated face-to-face interview. The telephone interview takes approximately 15 min and includes a selection of key indicators of functioning. Sampling, response, and procedures are described in detail elsewhere [15]. For the current study, data from 2008–2009 (T1) and 2011–2012 (T2) were used. At T1, 1,818 respondents participated, aged 60.9–100.6 years. We excluded those who did not participate at T2 (drop-out between T1 and T2, $n = 296$) and those who only had a telephone interview at T2 and, therefore, did not have a score on the LASA-FI ($n = 219$). Those excluded due to lack of follow-up were more often frail at baseline, lower educated, and older than those with a follow-up

Fig. 1. Histogram showing the distribution of the LASA-FI.

measurement. Furthermore, we excluded respondents who were not 75 years or over at T2 ($n = 734$). We ended up with a sample of 569 respondents.

Measures

Outcomes

Our outcome measures were frailty and vitality at T2. They were measured with the LASA-FI [16]. The LASA-FI includes 32 health deficits, including self-reported chronic conditions (11 items), functional limitations (6 items), self-rated health (2 items), mental health (6 items), physical performance measured by gait speed (1 item), self-reported memory complaints (5 items), and physical activity (1 item). An overview of all included items and cutoff values can be found elsewhere [16]. All deficits were scored 0 or 1, where 0 indicates the absence of the deficit and 1 the presence of a deficit. Frailty scores were calculated for each respondent with 20% or less missing variables of the LASA-FI. The sum of the health deficit scores was divided by the total number of health deficits measured. This resulted in a score between 0 (no deficits present) and 1 (all deficits present). The distribution of the LASA-FI can be found in Figure 1. We applied the generally used cutoff point of ≥ 0.25 [17] to identify respondents who were frail. The recommended cutoff point to identify “fit” older adults usually corresponds to the presence of a maximum of 4 to 5 deficits [18]. Using the LASA-FI, a cutoff of ≤ 0.15 corresponds to 4 to 5 deficits and was, therefore, used to identify respondents who were vital. The mean number of deficits in the vital group using this cutoff was 3.2 ($SD = 1.12$), while the mean number of deficits in the frail group was 11.9 ($SD = 3.0$).

Candidate Predictors

We used candidate predictors from the following domains: the sociodemographic, lifestyle, social, psychological, and physical domains. An FI does not specify which (combination of) deficits must be present for someone to be considered frail. Rather, it is the accumulation of deficits that matters. The FI is largely indifferent to its underlying items [19], thus including predictors that are also part of the index is not problematic. Furthermore, predictors were measured at T1, while frailty/vitality was measured at T2.

Sociodemographic Factors

We included sex, age, educational level (years of education), partner status (partner no/yes), having children (no/yes), having a job (no/yes), and income. To assess the income of the household, respondents were asked what their monthly household income was, choosing from 24 categories, with the lowest category being EUR 454–567 and the highest category EUR 5,446 or more. To ensure comparability of income between persons with and without a partner in the household, income was multiplied by 0.7 for respondents with a partner in the household. Income was categorized into tertiles.

Lifestyle Factors

Respondents were asked about their smoking and drinking habits. Smoking was categorized as nonsmoker, former smoker, or current smoker. Respondents were also asked how many days per week they drink alcohol and how many consumptions they drink each time. We calculated the number of glasses per day and used sex-specific cutoffs to categorize alcohol use into no use, moderate use (M: 1–3 drinks and F: 1–2 drinks), and excessive use (M: 4 + drinks and F: 3 + drinks).

Physical activity was measured with the LASA Physical Activity Questionnaire (LAPAQ) [20]. Respondents were asked about the frequency and duration of various activities during the previous 2 weeks. Activities include walking outside, doing light and heavy household work, cycling, gardening, and a maximum of 2 sports. The WHO recommends older adults to engage in moderately intensive physical activities for at least 150 min throughout the week [21]. We categorized respondents as physically inactive if they did not meet this recommendation and as physically active if they did.

Respondents were asked about their sleep problems in the self-administered questionnaire. They were asked whether they had problems with falling asleep, waking up in the night, or waking up too early in the morning, with 4 response categories ranging from (1) almost never to (4) almost always. A sum score was calculated ranging from 3 (no problems) to 12 (many problems).

Social Factors

Loneliness was assessed using the De Jong-Gierveld Loneliness Scale, which ranges from 0 to 11 [22]. Respondents were considered to be lonely when they had a score of 3 or higher.

Respondents were asked to name the persons they were in frequent contact with and who were also important to them. By doing so, the size of the social network was identified (0–80).

Respondents were also asked how much instrumental and emotional support they received from the 9 most frequently contacted persons from their social network. Response possibilities were (1) never, (2) seldom, (3) sometimes, and (4) often. A sum score (0–36) was calculated, with higher scores indicating more support.

We included 3 types of informal and formal social participation: participating in leisure activities and membership and volunteering in community organizations. Respondents indicated how often ((1) almost never, (2) a few times a year, (3) every month, (4) a few times a month, (5) every week, (6) a few times a week, and (7) every day) they engaged in 7 leisure activities (e.g., visiting a museum, going to a bar/restaurant, shopping for pleasure). Respondents were considered to engage in leisure activities if they engaged in at least 1 leisure activity at least every month (except for shopping, which had to be at least once a week). Furthermore, respondents indicated whether they were members of 12 types of community organizations, ranging from a church, trade unions, and sports organizations to choirs. A variable was created for whether respondents were a member of a community organization (no/yes, member of at least one of these organizations). Those who were members were asked whether they carried out volunteer work in the community organization (no/yes).

Psychological Factors

Mastery was measured with the Pearlin Mastery Scale [23], which consists of 7 items measuring the extent to which one regards one's life-chances as being under one's own control. Answer categories range from (1) strongly disagree to (5) strongly agree. Sum scores ranged from 7 to 35, with higher scores indicating a higher sense of mastery.

Self-efficacy was measured with the General Self-Efficacy Scale (GSES), constructed by Sherer et al. [24]. In LASA, an abbreviated version was used, consisting 12 items [25]. These items cover 3 different aspects: willingness to initiate behavior, persistence when facing adversity, and effort to complete behavior. Respondents could answer each question on a 5-point scale ranging from (1) strongly disagree to (5) strongly agree. Sum scores ranged from 12 to 60, with higher scores reflecting more self-efficacy.

Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CES-D) [26]. The CES-D is a 20-item self-report scale ranging from 0 to 60, with higher scores reflecting more depressive symptoms.

Anxiety was measured with the Hospital Anxiety and Depression Scale-Anxiety (HADS-A) [27]. The HADS-A is a 7-item self-report questionnaire. The scale ranges from 0 to 21, with higher scores indicating higher levels of anxiety.

Cognitive functioning was measured using the Mini-Mental State Examination (MMSE) [28]. The MMSE consists of 23 items and scores range from 0 to 30, with higher scores reflecting better cognitive functioning. Respondents were also asked whether they had memory complaints (no/yes).

Physical Factors

Grip strength was measured using a JAMAR 5030J1 Hydraulic Hand Dynamometer. Respondents were instructed to perform 2 maximum grip strength trials with each hand. The mean of the highest score of the left and right hand was calculated, and the sex- and BMI-specific lowest quintile was categorized as “weak grip strength.”

Blood pressure was measured twice, with significant time between the measurements, using an automatic Omron device (Omron HEM 815F). All measurements were performed at the upper left arm. When this was not possible, the right arm was used. Respondents were not allowed to smoke, eat, or be physically active during the last hour before the measurement. Respondents were categorized as having hypertension with a systolic blood pressure of >150 mm Hg and/or a diastolic blood pressure of >90 mm Hg.

Height and weight were also measured during the visit. BMI was calculated and categorized into normal weight (<25), overweight (25–30), and obese (≥30). Because only 3 respondents were underweight (BMI < 18.5), this category was collapsed with the normal weight category.

Respondents were asked about their medication use. Polypharmacy was categorized as no (<5 medications) or yes (≥5 medications).

To measure hearing problems, respondents were asked whether they could follow a conversation in a group of 3 or 4 persons with and without a hearing aid, and whether they could follow a conversation with 1 person with and without a hearing aid. Response categories were (1) yes, without difficulty, (2) yes, but with some difficulty, (3) yes, but with much difficulty, and (4) no, I cannot. Respondents were categorized as having hearing problems if they had at least some difficulty with more than one of these items. To measure vision problems, respondents were asked whether they could read small letters of the newspaper with and without glasses or contact lenses and whether they could recognize someone's face at 4 meters with and without glasses or contact lenses. Response categories and categorization were the same as for hearing problems.

The number of chronic diseases was measured by self-reports of the following 7 chronic diseases: chronic nonspecific lung disease, cardiovascular diseases, peripheral artery diseases, diabetes mellitus, stroke, arthritis, and malignancies. Self-rated health (SRH) was measured with the question “How is your health in general?” and respondents could answer on a 5-point Likert scale ranging from (1) very good to (5) poor. Responses were dichotomized into (0) very good/good SRH or (1) less than good SRH.

Five items measuring pain were included in the self-administered questionnaire: I am in pain when I am standing, I find it painful to change position, I am in pain when I am sitting, I am in pain when I walk, and I am in constant pain [29]. Response categories were (1) no and (2) yes. Sum scores were calculated ranging from 5 (no symptoms of pain) to 10 (5 symptoms of pain).

Statistical Analysis

We used the multivariate imputation by chained equations package in R statistical software [30] to multiply impute missing values in the predictor variables. When including all candidate predictor variables, the dataset contained 37% incomplete cases, and therefore, 37 imputed datasets were generated [31]. Missingness at random was assumed.

We used logistic regression analyses to first examine univariable associations between the predictors and the outcomes. Then, full multivariable logistic regression models were reduced using backward stepwise selection, with an exclusion criterion of $\alpha = 0.05$. We used the *psfmi* package in R [32], in which variable selection was based on Rubin's rules for pooled estimates.

Because prediction models generally perform better in the sample used to develop the model than in an external sample, shrinkage factors can be used to correct for this optimism [33]. If the calibration slope of a model is lower than 1, this reflects overfitting and it can be interpreted as reflecting the need for shrinkage of the coefficients. The regression coefficients in the full model were adjusted for optimism using the "pool_intadj" function in the *psfmi* package. We used the function "psfmi_perform" to evaluate the performance of the models in the multiply imputed datasets. First, bootstrap samples were drawn from each imputed dataset before results were combined [34]. The Nagelkerke's *R*-square, corrected for optimism, was used as a measure for the overall predictive performance of the models. The degree of discrimination of the models, that is, the ability to discriminate between older adults who are and those who are not frail/vital, was evaluated with the area under the ROC-curve (AUC). An AUC < 0.60 reflects failing, 0.60–0.69 poor, 0.70–0.79 fair, 0.80–0.89 good, and ≥ 0.90 excellent discrimination [35]. The AUC was corrected for optimism in each imputed dataset, and a pooled estimate was presented. All analyses were performed in R version 3.6.1. In reporting our prediction models, we followed the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement [36].

Results

Table 1 shows the characteristics of the sample. In our sample, 49.4% were considered to be frail and 18.3% were considered to be vital at follow-up. When we stratified by age-group, we found a prevalence of 36.1% in the 75–79 age-group, 47.9% in the 80–84 age-group, and 69.4% in the 85 + age-group for frailty, and 26.9, 17.4, and 17.4%, respectively, for vitality.

In Table 2, the estimates of the univariable regression analyses can be found, as well as the optimism adjusted estimates of the final models. The final model predicting vitality included: age, sex, alcohol use, received emotional support, depressive symptoms, hearing problems, number of chronic diseases, and SRH. The calibration slope of this model was 0.76, which was used to adjust the model for overfitting. The final model explained 42% of the variance in vitality, after adjustment for optimism. The optimism adjusted AUC was 0.88, showing good discriminative value.

We found that age, depressive symptoms, number of chronic diseases, and SRH were also predictors in the final model predicting frailty. In addition, cognitive functioning, polypharmacy, and pain remained in the final

prediction model. The calibration slope for this model was 0.82 and the model explained 48% of the variance, after adjustment for this optimism. The frailty model also had a good discriminative value, with an optimism adjusted AUC of 0.85.

Sensitivity Analyses

In our sample, 31% of those who were frail at T2 were also frail at T1 and 14% were vital at both T1 and T2. To ensure baseline frailty and vitality status did not affect our models, we conducted sensitivity analyses in which we adjusted the prediction models for baseline frailty and vitality status. These analyses yielded similar prediction models.

Discussion

The number of older adults aged 75 years and over will strongly increase in the coming decades. This particular age-group is not only more at risk of frailty but also seems to be at higher risk of adverse outcomes due to frailty [13, 14]. Identifying older adults at risk of frailty or vitality could guide health and social care professionals in appropriate use of health and social care resources and implementation of person-oriented preventive strategies. It has been suggested that early intervention initiatives would be best situated within a setting where older people feel comfortable, for example, in their own homes, at their GP practice, or at facilities they visit regularly [37]. Therefore, it is important to identify a set of predictors that can be easily measured in such a setting.

The prevalence of frailty at follow-up in our sample was 49.4%. Frailty prevalence rates vary greatly between studies, depending on the countries where the studies were conducted, the age of the sample, and measurements used [38]. Studies using the FI, which is a multidimensional frailty measure, generally report higher prevalence compared to studies using the physical frailty phenotype (Fried criteria), another widely used frailty construct. The prevalence found in our study is consistent with another Dutch study estimating the prevalence of frailty between 40.2 and 59.1%, depending on the measure, in older adults aged 70 years and over [39]. The prevalence of frailty increases substantially with age, explaining the rather high prevalence of frailty in our sample with a mean age of 79.4 years. The prevalence of vitality was 18.3% in our sample, and the mean number of deficits in these vital older adults was 3.2. This means that almost one-fifth of older adults aged 75 years and over did

Table 1. Characteristics of the sample ($n = 569$)

		% Missing values before multiple imputation
Frailty, %	49.4	0.0
Vitality, %	18.3	0.0
Age (range 71.8–99.0), mean (SD)	79.4 (5.4)	0.0
Sex (women), %	59.4	0.0
Education (range 5–18), mean (SD)	9.5 (3.3)	0.0
Income, %		
Lowest tertile	35.9	11.8
Middle tertile	32.5	
Highest tertile	31.6	
Having children, %	88.7	0.0
Partner status (having a partner), %	56.6	0.0
Having a job, %	4.5	6.0
Smoking, %		
Never	37.1	7.2
Former smoker	56.6	
Current smoker	6.3	
Alcohol use, %		
No use	34.5	7.9
Moderate use	16.8	
Excessive use	48.7	
Sleep problems (range 3–12), mean (SD)	6.0 (2.1)	8.3
Physical activity (physically active), %	64.9	0.0
Emotional support (range 0–36), mean (SD)	22.5 (7.5)	6.9
Instrumental support (range 0–34), mean (SD)	16.0 (6.1)	6.7
Social network size (range 0–64), mean (SD)	15.9 (9.4)	6.7
Loneliness (lonely), %	32.7	3.2
Participating in leisure activities, %	67.5	0.0
Membership of organization, %	70.8	0.0
Volunteering, %	30.6	9.8
Self-efficacy (range 23–60), mean (SD)	41.6 (5.3)	6.3
Mastery (range 7–25), mean (SD)	16.9 (3.4)	6.5
Anxiety (range 0–17), mean (SD)	2.8 (2.9)	3.2
Depressive symptoms (range 0–40), mean (SD)	8.1 (6.9)	3.2
Cognitive functioning (range 13–30), mean (SD)	27.4 (2.4)	3.2
Memory complaints, %	34.9	3.2
Hearing problems, %	20.1	9.1
Vision problems, %	75.9	10.9
BMI, %		
Normal weight	27.2	10.9
Overweight	45.6	
Obese	27.2	
Chronic diseases (range 0–6), mean (SD), n	1.7 (1.1)	3.2
Polypharmacy, %	39.6	7.2
Less than good SRH, %	39.9	3.5
Pain (range 5–10), mean (SD)	6.0 (1.5)	11.4
Weak grip strength, %	16.9	12.5
Hypertension, %	24.8	11.8
SRH, self-rated health.		

Table 2. Univariable estimates and estimates in the final model predicting vitality and frailty

	Vitality OR (95% CI)		Frailty OR (95% CI)	
	univariable regression	final model ^a	univariable regression	final model ^a
Age	0.89 (0.84–0.93)	0.93 (0.86–0.97)	1.12 (1.08–1.16)	1.10 (1.07–0.01)
Sex (women)	0.45 (0.29–0.69)	0.39 (0.16–0.56)	2.10 (1.49–2.95)	
Education	1.14 (1.07–1.22)		0.89 (0.84–0.94)	
<i>Income</i>				
Lowest tertile	<i>R</i>		<i>R</i>	
Middle tertile	1.48 (0.81–2.69)		0.95 (0.62–1.46)	
Highest tertile	2.49 (1.42–4.38)		0.38 (0.24–0.60)	
Having children	1.74 (0.77–3.94)		0.82 (0.48–1.41)	
Partner status (having a partner)	1.74 (1.11–2.73)		0.48 (0.35–0.68)	
Having a job	2.87 (1.27–6.45)		0.78 (0.35–1.69)	
<i>Smoking</i>				
Never	<i>R</i>		<i>R</i>	
Former smoker	1.44 (0.89–2.32)		0.57 (0.40–0.81)	
Current smoker	1.71 (0.72–4.06)		0.88 (0.43–1.83)	
<i>Alcohol use</i>				
No use	<i>R</i>	<i>R</i>	<i>R</i>	
Moderate use	1.46 (0.75–2.84)	1.80 (0.90–5.17)	0.84 (0.51–1.40)	
Excessive use	1.49 (0.90–2.44)	0.80 (0.38–1.48)	0.68 (0.47–0.98)	
Sleep problems	0.80 (0.71–0.90)		1.24 (1.14–1.36)	
Physical activity (physically active)	3.07 (1.79–5.28)		0.26 (0.18–0.37)	
Emotional support	1.03 (1.00–1.06)	1.04 (1.01–1.09)	1.00 (0.97–1.02)	
Instrumental support	0.99 (0.96–1.03)		1.03 (1.01–1.06)	
Social network size	1.04 (1.02–1.06)		0.96 (0.94–0.98)	
Loneliness (lonely)	0.45 (0.26–0.75)		2.77 (1.91–4.01)	
Participating in leisure activities	1.45 (0.88–2.38)		0.59 (0.41–0.85)	
Membership of organization	1.57 (0.91–2.72)		0.67 (0.45–0.98)	
Volunteering	2.14 (1.36–3.36)		0.51 (0.35–0.74)	
Self-efficacy	1.10 (1.05–1.15)		0.92 (0.89–0.95)	
Mastery	1.12 (1.04–1.20)		0.86 (0.81–0.91)	
Anxiety	0.76 (0.68–0.85)		1.28 (1.19–1.38)	
Depressive symptoms	0.83 (0.79–0.88)	0.90 (0.82–0.94)	1.17 (1.13–1.21)	1.09 (1.06–1.16)
Cognitive functioning	1.16 (1.04–1.30)		0.85 (0.79–0.92)	0.88 (0.77–0.95)
Memory complaints	0.38 (0.22–0.64)		2.17 (1.51–3.10)	
Hearing problems	0.18 (0.07–0.45)	0.26 (0.06–0.55)	3.00 (1.89–4.78)	
Vision problems	0.58 (0.36–0.95)		1.31 (0.86–1.98)	
<i>BMI</i>				
Normal weight	<i>R</i>		<i>R</i>	
Overweight	0.75 (0.45–1.25)		1.01 (0.66–1.54)	
Obese	0.45 (0.24–0.85)		2.42 (1.49–3.92)	
Chronic diseases, <i>n</i>	0.21 (0.15–0.30)	0.35 (0.17–0.37)	2.78 (2.23–3.47)	1.58 (1.32–2.34)
Polypharmacy	0.21 (0.11–0.38)		4.76 (3.26–6.94)	2.14 (1.53–4.19)
Less than good SRH	0.09 (0.04–0.19)	0.36 (0.11–0.64)	8.18 (5.46–12.26)	2.43 (1.76–4.98)
Pain	0.47 (0.34–0.65)		1.87 (1.60–2.19)	1.33 (1.18–1.71)
Weak grip strength	0.36 (0.17–0.77)		2.13 (1.34–3.38)	
Hypertension	0.73 (0.43–1.23)		1.09 (0.75–1.60)	

ORs in bold indicate statistical significance ($p < 0.05$). SRH, self-rated health. ^a ORs corrected for optimism.

not experience a decrease in physiological reserve in multiple domains of functioning. This finding emphasizes the heterogeneity in older adults and the need to not only focus on frailty but to consider the entire continuum from fit to frail.

Almost all of our 33 candidate predictors were univariably associated with frailty and vitality. After backward stepwise selection, prediction models for both frailty and vitality included age, depressive symptoms, number of chronic diseases, and SRH. We also found differences between the models for vitality and frailty. Male sex, moderate alcohol use, more emotional support received, and no hearing problems were all predictors of being vital after 3 years. Lower cognitive functioning, polypharmacy, and having more pain were predictors of frailty after 3 years. Both prediction models explained a moderate percentage of variance (vitality: 42% and frailty: 48%), and the discriminative value of both models was good, that is, the models were able to discriminate well between older adults who were frail/vital and those who were not. These findings are supported by earlier research examining factors associated with frailty [2, 9, 10] and vitality [8]. Ng et al. [10] developed a prediction model for frailty in Singapore for a younger age-group (55+), and also found age, depressive symptoms, and chronic diseases to be predictors of frailty. To our knowledge, we are the first to develop and validate prediction models for frailty and vitality in European older adults using such a broad set of predictors.

Our study has some limitations. First, we were not able to externally validate the prediction models. We did internally validate the models using bootstrapping techniques, but because bootstrap samples are derived from the same dataset, this only partially solves the problem of optimism. Therefore, external validation is recommended in future research. Second, the low percentage of vital older adults in our sample led to a low events-per-variable (EPV). While an EPV of 10 is generally recommended, a recent study concluded that the evidence for this criterion is weak [40], suggesting that a violation of this EPV recommendation may not necessarily lead to biased results. As our prediction models were stable, we expect that exceeding the recommended EPV did not influence the performance of our models. Third, we operationalized vitality as having less than 5 (out of 32) deficits, using the LASA-FI. Thus, we only considered the absence of deficits rather than the presence of positive traits. While the use of an FI to identify both frail and vital older adults has practical advantages, further research is needed to assess whether vitality operationalized in this way is indeed associated with a higher risk of positive outcomes and a

lower risk of adverse outcomes. While for frailty the FI methodology considers each item in the FI as equal, it is possible that for vitality the absence of some deficits may be more important than others. For example, to remain vital, the absence of mobility limitations may be more important than the absence of a disease that can be easily controlled with medication. Therefore, in future studies, other cutoffs as well as the option of weighting items should be examined when using the FI to measure vitality. Finally, we included predictors that were also included in the FI: chronic diseases, several items of the CES-D (depressive symptoms), physical activity, memory complaints, and several items of the MMSE (cognitive functioning). However, previous studies have shown that this is not problematic, since the FI is largely indifferent to its underlying items [19]. It is the accumulation of deficits that matters, rather than the presence of specific (combinations of) deficits.

Strengths of our study include the use of a representative sample of Dutch older adults, inclusion of predictors from multiple domains, and internal validation of our models. Also, the predictors included in our study can all be measured relatively easily in different settings, and no laboratory tests are needed. In addition, we focused not only on frailty but also on vitality, which so far has been largely neglected in research on older adults.

In conclusion, it is important to not only focus on frailty in older adults but also on the other end of the spectrum, that is, vitality, to take into account the heterogeneity in older adults. Our study shows that although predictors of vitality and frailty partially overlap, there are indeed differences in the final prediction models, suggesting conceptual differences between vitality and frailty. We found that predictors of frailty and vitality encompassed several domains, with predictors in the physical domain being most dominantly present. The readily accessible predictors in our models may help to easily identify older adults who are likely to be vital and who are at risk of frailty.

Statement of Ethics

This study received approval by the Medical Ethics Committee of the VU University medical center. Signed informed consent was obtained from all study participants.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

Funding Sources

This study was supported by a grant from the SeW Foundation. The Longitudinal Aging Study Amsterdam is largely supported by a grant from the Netherlands Ministry of Health, Welfare and Sports, Directorate of Long-Term Care. Emiel O. Hoogendijk was supported by an NWO/ZonMw Veni fellowship [grant number 91618067].

Author Contributions

Sascha de Breij and Emiel O. Hoogendijk were responsible for the design of the study. Sascha de Breij analyzed and interpreted the data and drafted the manuscript. All authors critically revised the research design and the manuscript. All authors approved the final version of the manuscript.

References

- Statline CBS, 2019, <http://statline.cbs.nl/Statweb>.
- Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. *Lancet*. 2019;394(10206):1365–75.
- Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: a review. *Eur J Intern Med*. 2016;31:3–10.
- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*. 2013;381(9868):752–62.
- Bortz WM II. The physics of frailty. *J Am Geriatr Soc*. 1993;41(9):1004–8.
- Rockwood K, Howlett SE, MacKnight C, Beattie BL, Bergman H, Hébert R, et al. Prevalence, attributes, and outcomes of fitness and frailty in community-dwelling older adults: report from the Canadian study of health and aging. *J Gerontol A Biol Sci Med Sci*. 2004;59(12):1310–7.
- Rockwood K, Song X, Mitnitski A. Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. *CMAJ*. 2011;183(8):E487–94.
- Minicuci N, Marzari C, Maggi S, Noale M, Senesi A, Crepaldi G. Predictors of transitions in vitality: the Italian longitudinal study on aging. *J Gerontol A Biol Sci Med Sci*. 2005;60(5):566–73.
- Feng Z, Lugtenberg M, Franse C, Fang X, Hu S, Jin C, et al. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: a systematic review of longitudinal studies. *PLoS One*. 2017;12(6):e0178383.
- Ng TP, Feng L, Nyunt MS, Larbi A, Yap KB. Frailty in older persons: multisystem risk factors and the Frailty Risk Index (FRI). *J Am Med Dir Assoc*. 2014;15(9):635–42.
- Belloni G, Cesari M. Frailty and intrinsic capacity: two distinct but related constructs. *Front Med*. 2019;6:133.
- Hoogendijk EO, Stenholm S, Ferrucci L, Bandinelli S, Inzitari M, Cesari M. Operationalization of a frailty index among older adults in the InCHIANTI study: predictive ability for all-cause and cardiovascular disease mortality. *Aging Clin Exp Res*. 2020;32(6):1025–34.
- Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. *J Epidemiol Community Health*. 2016;70(7):722–9.
- de Vries OJ, Peeters GM, Lips P, Deeg DJ. Does frailty predict increased risk of falls and fractures? A prospective population-based study. *Osteoporos Int*. 2013;24(9):2397–403.
- Hoogendijk EO, Deeg DJH, de Breij S, Klokgieters SS, Kok AAL, Stringa N, et al. The Longitudinal Aging Study Amsterdam: cohort update 2019 and additional data collections. *Eur J Epidemiol*. 2020;35(1):61–74.
- Hoogendijk EO, Theou O, Rockwood K, Onwuteaka-Philipsen BD, Deeg DJH, Huisman M. Development and validation of a frailty index in the Longitudinal Aging Study Amsterdam. *Aging Clin Exp Res*. 2017;29(5):927–33.
- Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci*. 2007;62(7):738–43.
- Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age Ageing*. 2016;45(3):353–60.
- Rockwood K, Mitnitski A, Song X, Steen B, Skoog I. Long-term risks of death and institutionalization of elderly people in relation to deficit accumulation at age 70. *J Am Geriatr Soc*. 2006;54(6):975–9.
- Stel VS, Smit JH, Pluijm SM, Visser M, Deeg DJ, Lips P. Comparison of the LASA physical activity questionnaire with a 7-day diary and pedometer. *J Clin Epidemiol*. 2004;57(3):252–8.
- World Health Organization. *Global recommendations on physical activity for health*. Geneva, Switzerland: WHO Press; 2010.
- de Jong-Gierveld J, Kamphuis F. The development of a Rasch-type loneliness scale. *Appl Psychol Meas*. 1985;9(3):289–99.
- Pearlin LI, Schooler C. The structure of coping. *J Health Soc Behav*. 1978;19(1):2.
- Sherer M, Maddux JE, Mercandante B, Prentice-Dunn S, Jacobs B, Rogers RW. The Self-efficacy Scale: construction and validation. *Psychol Rep*. 1982;51(2):663–71.
- Boscher RJ, Smit JH. Confirmatory factor analysis of the General Self-Efficacy Scale. *Behav Res Ther*. 1998;36(3):339–43.
- Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385–401.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361–70.
- Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–98.
- Hunt SM, McEwen J, McKenna SP. Measuring health status: a new tool for clinicians and epidemiologists. *J R Coll Gen Pract*. 1985;35(273):185–8.
- Van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. *J Stat Software*. 2010:1–68.
- White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med*. 2011;30(4):377–99.
- Heymans MW, Eekhout I. psfmi: predictor selection functions for logistic and cox regression models in multiply imputed datasets. 2020.
- Steyerberg EW. *Clinical prediction models*. Berlin: Springer; 2019.
- Marshall A, Altman DG, Holder RL, Royston P. Combining estimates of interest in prognostic modelling studies after multiple imputation: current practice and guidelines. *BMC Med Res Methodol*. 2009;9:57.
- Fan J, Upadhye S, Worster A. Understanding receiver operating characteristic (ROC) curves. *CJEM*. 2006;8(1):19–20.
- Moons KG, Altman DG, Reitsma JB, Ioannidis JP, Macaskill P, Steyerberg EW, et al. Transparent Reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): explanation and elaboration. *Ann Intern Med*. 2015;162(1):W1–73.
- Lette M, Stoop A, Lemmens LC, Buist Y, Baan CA, de Bruin SR. Improving early detection initiatives: a qualitative study exploring perspectives of older people and professionals. *BMC Geriatr*. 2017;17(1):132.
- Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc*. 2012;60(8):1487–92.
- Metzelsch SF, Daniëls R, van Rossum E, de Witte L, van den Heuvel WJ, Kempen GI. The psychometric properties of three self-report screening instruments for identifying frail older people in the community. *BMC Public Health*. 2010;10(1):176.
- van Smeden M, de Groot JA, Moons KG, Collins GS, Altman DG, Eijkemans MJ, et al. No rationale for 1 variable per 10 events criterion for binary logistic regression analysis. *BMC Med Res Methodol*. 2016;16(1):163.