**Supplementary Information for the Submission by Amblàs-Novellas et al. "Frailty Degree and Illness Trajectories in Older People towards the End-of-life: A Prospective Observational Study".**

# Supplementary Methods

*Construction of the Cox Proportional Hazards Model and Calculation of Hazard Ratios*

A Cox Proportional Hazards (PH) model was constructed considering a multiplicative interaction between the Frail-VIG index and the qualitative variable "illness trajectory" (dementia was set as the reference category); see the estimation results in Table S1. When the model was constructed considering sex and age as covariates, sex lacked statistical significance (Table S2) and, similarly, upon removal of sex from the model, age lacked statistical significance (Table S3). Consequently, sex and age were excluded and Frail-VIG index score and Illness trajectories were the only covariates that remained in the final Cox PH model (Table S1).

To calculate hazard ratios for each illness trajectory, each hazard ratio was computed as the exponential of the sum of the coefficient of the Frail-VIG index (11.99) and each interaction coefficient (0, -5.41, -5.51, -8.96), yielding hazard ratios for one unit increase in the Frail-VIG index (Table S4). However, as Frail-VIG index scores are expressed as 0.04 increments for each additional deficit of a total of 25 deficits (1/25=0.04), hazard ratios were subsequently raised to 0.04, to calculate hazard ratios consistent with the units of Frail-VIG index scores (Table S5).

Supplemental material

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# Supplementary Tables

**Table S1.** Cox Proportional Hazards fit

| Variable | Beta | SE | z | P | 95% CI |
|---|---|---|---|---|---|
| **Frail-VIG index score** | 11.99 | 1.48 | 8.09 | **<0.001** | (9.08, 14.89) |
| **Illness trajectory** | | | | | |
| Dementia (ref) | - | - | - | - | - |
| Organ Failure | 3.75 | 1.05 | 3.56 | **<0.001** | (1.69, 5.82) |
| Multimorbidity | 3.48 | 1.08 | 3.23 | **0.001** | (1.37, 5.60) |
| Cancer | 5.69 | 1.12 | 5.10 | **<0.001** | (3.50, 7.87) |
| **Frail-VIG index by trajectory** | | | | | |
| Organ Failure | -5.41 | 1.82 | -2.98 | **0.003** | (-8.97, -1.85) |
| Multimorbidity | -5.51 | 1.80 | -3.07 | **0.002** | (-9.02, -1.99) |
| Cancer | -8.96 | 1.96 | -4.57 | **<0.001** | (-12.80, -5.12) |

**Table S2.** Cox Proportional Hazards fit with sex and age

| Variable | Beta | SE | z | P | 95% CI |
|---|---|---|---|---|---|
| **Frail-VIG index score** | 11.91 | 1.46 | 8.14 | **<0.001** | (9.04, 14.78) |
| **Illness trajectory** | | | | | |
| Dementia (ref) | - | - | - | - | - |
| Organ Failure | 3.44 | 1.05 | 3.26 | **0.001** | (1.37, 5.50) |
| Multimorbidity | 3.13 | 1.07 | 2.92 | **0.003** | (1.03, 5.23) |
| Cancer | 5.80 | 1.09 | 5.32 | **<0.001** | (3.66, 7.94) |
| **Sex** | | | | | |
| Female (ref) | - | - | - | - | - |
| Male | 0.22 | 0.14 | 1.62 | 0.11 | (-0.05, 0.49) |
| **Age** | 0.03 | 0.01 | 2.20 | **0.03** | (0.00, 0.05) |
| **Frail-VIG by trajectory** | | | | | |
| Organ Failure | -4.96 | 1.81 | -2.74 | **0.006** | (-8.52, -1.41) |
| Multimorbidity | -5.01 | 1.78 | -2.82 | **0.005** | (-8.49, -1.53) |
| Cancer | -9.35 | 1.92 | -4.88 | **<0.001** | (-13.11, -5.59) |

**Table S3.** Cox Proportional Hazards fit with age

| Variable | Beta | SE | z | P | 95% CI |
|---|---|---|---|---|---|
| **Frail-VIG index score** | 11.94 | 1.48 | 8.09 | **<0.001** | (9.05, 14.83) |
| **Illness trajectory** | | | | | |
| Dementia (ref) | - | - | - | - | - |
| Organ Failure | 3.57 | 1.05 | 3.39 | **<0.001** | (1.50, 5.64) |
| Multimorbidity | 3.18 | 1.08 | 2.94 | **0.003** | (1.06, 5.30) |
| Cancer | 5.77 | 1.11 | 5.21 | **<0.001** | (3.60, 7.95) |
| **Age** | 0.02 | 0.01 | 1.99 | 0.05 | (0.00, 0.05) |
| **Frail-VIG by trajectory** | | | | | |
| Organ Failure | -5.12 | 1.82 | -2.82 | **0.005** | (-8.68, -1.56) |
| Multimorbidity | -5.06 | 1.79 | -2.82 | **0.005** | (-8.57, -1.55) |
| Cancer | -9.17 | 1.95 | -4.71 | **<0.001** | (-12.98, -5.35) |

**Table S4.** Hazard ratios for one unit increase in the Frail-VIG index

| Variable | Hazard Ratio | Lower | Upper | *P*-value |
|---|---|---|---|---|
| Dementia | 160727.38 | 8807.45 | 2933118.39 | 0.00 |
| Organ Failure | 717.52 | 64.17 | 8023.37 | 0.00 |
| Multimorbidity | 652.87 | 62.60 | 6808.63 | 0.00 |
| Cancer | 20.66 | 1.47 | 290.10 | 0.02 |

**Table S5.** Hazard ratios for a 0.04 unit increase in the Frail-VIG index

| Variable | Hazard Ratio | Lower | Upper | *P*-value |
|---|---|---|---|---|
| Dementia | 1.62 | 1.44 | 1.81 | 0.00 |
| Organ Failure | 1.30 | 1.18 | 1.43 | 0.00 |
| Multimorbidity | 1.30 | 1.18 | 1.42 | 0.00 |
| Cancer | 1.13 | 1.02 | 1.25 | 0.02 |