

SUPPLEMENTARY DATA

Appendix 1- Prevalence (and 95% CI) of all deficits (n=30) included in the frailty index by study as a percentage.

Deficit	Prevalence % (95% CI)						% Relative change
	CFAS I			CFAS II			
Medical conditions							
Angina	17.2	(16.3,	18.0)	16.0	(15.2,	16.9)	-1.2
Arthritis	53.0	(51.8,	54.1)	54.1	(52.9,	55.2)	1.1
Depression ^a	10.4	(9.7,	11.1)	7.4	(6.8,	8.0)	-3.0
Diabetes mellitus	6.3	(5.7,	6.8)	14.5	(13.6,	15.3)	8.2
Epileptic Fits	2.1	(1.8,	2.5)	2.2	(1.9,	2.6)	0.1
Head injury	12.3	(11.6,	13.1)	11.3	(10.5,	12.0)	-1.0
Heart attack	10.2	(9.5,	10.8)	11.4	(10.7,	12.2)	1.2
Intermittent claudication	4.3	(3.8,	4.8)	2.8	(2.4,	3.2)	-1.5
Medicated hypertension	26.4	(25.4,	27.4)	50.2	(49.0,	51.3)	23.8
Meningitis or encephalitis	0.8	(0.6,	1.0)	2.0	(1.7,	2.3)	1.2
Parkinson's disease	1.1	(0.8,	1.3)	0.9	(0.7,	1.1)	-0.2
Peptic ulcers	10.2	(9.5,	10.9)	8.4	(7.8,	9.1)	-1.8
Stroke	7.9	(7.3,	8.5)	8.6	(7.9,	9.3)	0.7
Thyroid problems	7.3	(6.7,	7.9)	12.9	(12.1,	13.6)	5.6
Transient ischaemic attack	14.7	(13.9,	15.5)	8.5	(7.8,	9.1)	-6.2
Other conditions							
Chairbound/Bedbound	2.0	(1.7,	2.3)	2.3	(1.9,	2.8)	0.3
Eyesight impairment	8.5	(7.9,	9.1)	6.6	(5.9,	7.3)	-1.9
Hearing difficulties	17.2	(16.3,	18.0)	17.4	(16.5,	18.3)	0.2
Poor cognition (MMSE <24)	23.0	(22.0,	24.0)	16.3	(15.3,	17.2)	-6.7
Poor self-reported health	6.8	(6.3,	7.4)	6.4	(5.8,	7.1)	-0.4
IADLs/ADLs^b							
Climb stairs	37.7	(36.6,	38.8)	37.5	(36.3,	38.7)	-0.2
Cook a hot meal	16.9	(16.0,	17.7)	18.3	(17.3,	19.2)	1.4
Do heavy housework	38.0	(36.8,	39.0)	46.7	(45.5,	47.8)	8.7
Get on a bus	28.8	(27.8,	29.8)	25.7	(24.6,	26.8)	-3.1
Reach an overhead shelf	29.8	(28.7,	30.8)	29.5	(28.4,	30.6)	-0.3
Shop and carry bags	47.2	(46.1,	48.3)	50.4	(49.3,	51.6)	3.2
Cut own toenails	43.7	(42.6,	44.9)	49.5	(48.3,	50.7)	5.8
Put on own shoes or socks	13.6	(12.8,	14.4)	22.3	(21.3,	23.3)	8.7
Take a bath	23.6	(22.6,	24.6)	22.8	(21.7,	23.8)	-0.8
Tie a knot	9.6	(8.9,	10.3)	12.0	(11.2,	12.9)	2.4

^a Depression is ever been diagnosed with depression by a doctor

^b Inability to perform (Instrumental) Activities of Daily Living (ADLs/IADLs).

Appendix 2- Mortality models for three analysis methods

	Model A ^a			Model B ^b			Model C ^c			Model D ^d			Final model ^e		
1) Complete case analysis															
Frailty Index	6.53	[5.02,	8.05]	4.12	[2.46,	5.76]	4.15	[2.50,	5.79]	4.20	[2.55,	5.85]	4.22	[2.57,	5.87]
Frailty Index squared	-2.11	[-4.80,	0.57]	0.75	[-2.09,	3.60]	0.69	[-2.15,	3.53]	0.61	[-2.24,	3.46]	0.57	[-2.26,	3.41]
Study	-0.38	[-0.51,	-0.24]	-0.48	[-0.62,	-0.35]	-0.69	[-0.88,	-0.50]	-3.01	[-4.48,	-1.55]	-2.85	[-4.31,	-1.38]
Sex			.	-0.67	[-0.82,	-0.53]	-0.90	[-1.08,	-0.72]	-0.67	[-0.81,	-0.52]	-0.84	[-1.02,	-0.67]
Age			.	0.08	[0.07,	0.09]	0.08	[0.07,	0.09]	0.06	[0.05,	0.07]	0.06	[0.05,	0.07]
Study by sex interaction			.			.	0.39	[0.12,	0.66]			.	0.31	[0.05,	0.58]
Study by age interaction			.			.			.	0.03	[0.01,	0.05]	0.03	[0.01,	0.05]
Constant	-3.50	[-3.70,	-3.31]	-8.77	[-9.53,	-7.99]	-8.67	[-9.45,	-7.90]	-7.28	[-8.21,	-6.37]	-7.40	[-8.32,	-6.47]
AUC	0.73			0.77			0.77			0.77			0.77		
2) ≥ 29 items answered															
Frailty Index	6.96	[5.48,	8.44]	4.53	[2.92,	6.09]	4.58	[2.97,	6.18]	4.62	[3.01,	6.23]	4.65	[3.04,	6.25]
Frailty Index squared	-2.68	[-5.26,	-0.10]	0.12	[-2.62,	2.86]	0.03	[-2.70,	2.76]	-0.02	[-2.76,	2.72]	-0.08	[-2.81,	2.65]
Study	-0.34	[-0.47,	-0.22]	-0.45	[-0.58,	-0.32]	-0.70	[-0.89,	-0.52]	-3.17	[-4.59,	-1.74]	-2.95	[-4.38,	-1.53]
Sex				-0.64	[-0.78,	-0.50]	-0.92	[-1.10,	-0.75]	-0.64	[-0.78,	-0.50]	-0.86	[-1.04,	-0.69]
Age				0.08	[0.07,	0.09]	0.08	[0.07,	0.09]	0.06	[0.05,	0.07]	0.06	[0.05,	0.07]
Study by sex interaction						.	0.47	[0.21,	0.73]			.	0.38	[0.12,	0.65]
Study by age interaction						.			.	0.03	[0.02,	0.05]	0.03	[0.01,	0.05]
Constant	-3.56	[-3.75,	-3.37]	-8.86	[-9.62,	-8.10]	-8.73	[9.49,	-7.97]	-7.23	[-8.12,	-6.35]	-7.37	[-8.27,	6.48]
AUC	0.73			0.77			0.78			0.78			0.78		

Appendix 2- Mortality models for three analysis methods (continued)

	Model A ^a			Model B ^b			Model C ^c			Model D ^d			Final model ^e		
3) MICE analysis															
Frailty Index	6.49	[4.97,	8.00]	4.86	[3.29,	6.43]	4.92	[3.35,	6.49]	4.98	[3.40,	6.55]	5.00	[3.43,	6.58]
Frailty Index squared	-2.03	[-4.74,	0.67]	-0.14	[-2.76,	2.47]	-0.23	[-2.84,	2.37]	-0.32	[-2.94,	2.29]	-0.37	[-2.98,	2.24]
Study	-0.38	[-0.51,	-0.25]	-0.39	[-0.51,	-0.27]	-0.66	[-0.84,	-0.49]	-2.97	[-4.29,	-1.65]	-2.73	[-4.05,	-1.41]
Sex			.			.	0.48	[0.24,	0.72]			.	-0.81	[-0.97,	-0.65]
Age			.			.			.	0.03	[0.02,	0.05]	0.07	[0.06,	0.08]
Study by sex interaction			.			.	0.48	[0.24,	0.72]			.	0.39	[0.14,	0.63]
Study by age interaction			.			.			.	0.03	[0.02,	0.05]	0.03	[0.01,	0.04]
Constant	-3.49	[-3.68,	-3.30]	-9.33	[-10.05,	-8.62]	-9.19	[-9.90,	-8.48]	-7.74	[-8.56,	-6.91]	-7.90	[-8.74,	-7.06]
AUC	0.75			0.79			0.79			0.79			0.79		

^a Model A: Frailty and Cohort change (study)

^b Model B: Frailty and Cohort change adjusted for sex and age differences

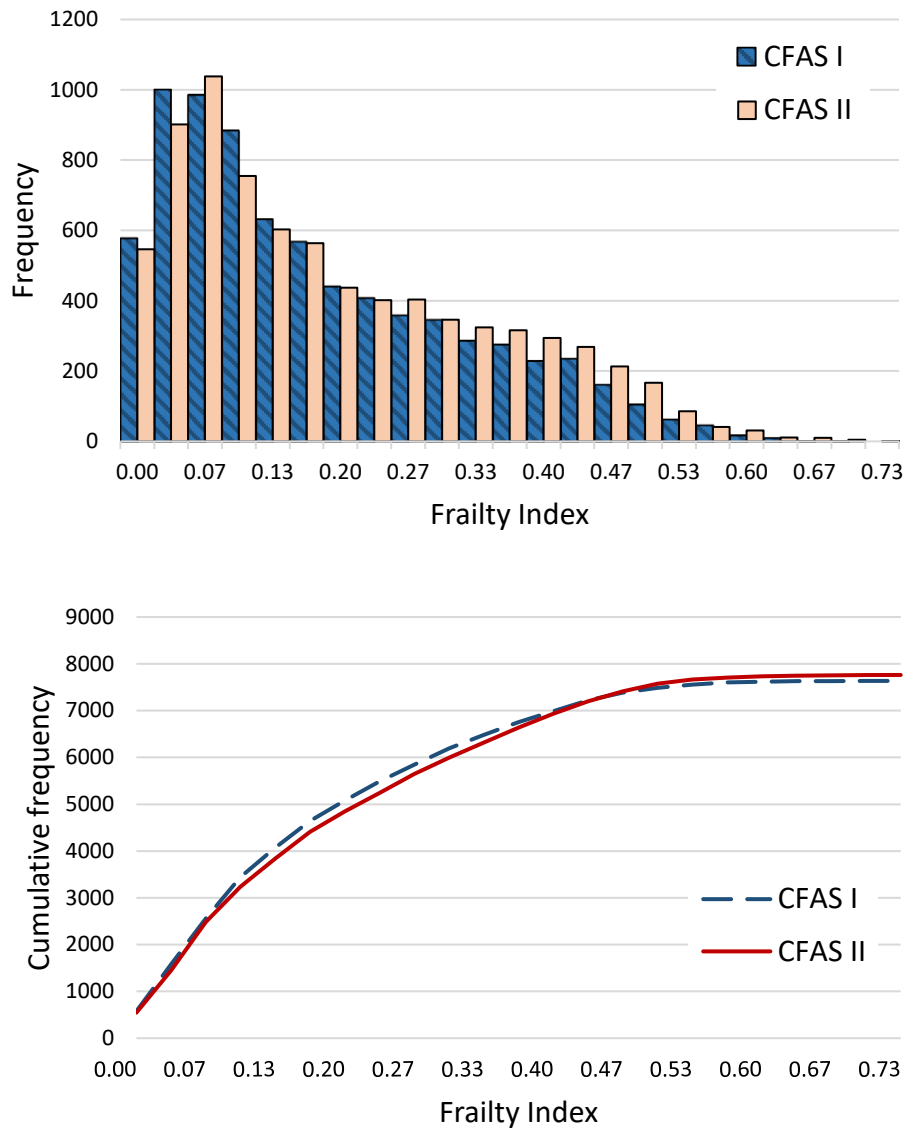
^c Model C: Model B + interaction between sex and cohort change

^d Model D: Model B + interaction between age and cohort change

^e Final model: Frailty and Cohort change adjusted for sex and age differences, and interactions between cohort change and sex and cohort and age

Note: The mortality models for the three analysis methods: complete case analysis (8.4% missing), inclusion of those who answered 29 items or more (5.1% missing) and multiple imputation analysis (with 10 iterations) using chained equations (all missing data imputed). The coefficient (β) for each predictor from the logistic regression model and its 95% Confidence Interval are also shown. The exponential of these coefficients ($\exp(\beta)$) correspond to the odds ratio of the covariate's effect. Negative coefficients will result to ORs between 0 and 1, showing a protective effect against mortality. Positive coefficients correspond to ORs over 1, showing greater odds of mortality. Frailty index was modelled as the proportion of deficits present. The reference category for study was CFAS I and the reference gender group was men. The area under the receiver operating characteristic curve (ROC-AUC) is also denoted as a measure of model discrimination in predicting 2-year mortality.

Appendix 3- A frequency distribution of the frailty index in CFAS I and II.

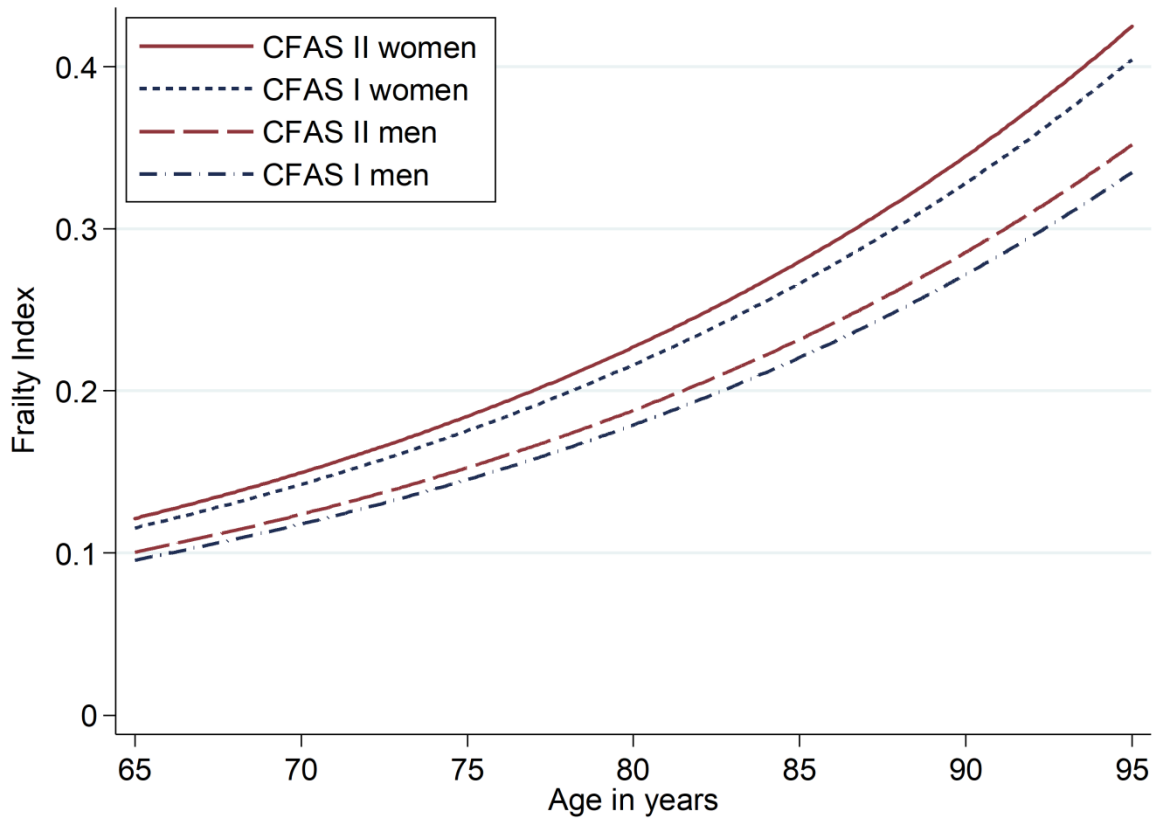


Note: The frequencies were obtained using non-response weights in a multiple imputation framework

Appendix 4 -Descriptive statistics of the frailty index and number of deaths by age bands and gender, for individuals aged 65 and over, Cambridgeshire, Newcastle and Nottingham, United Kingdom, 1991 (CFAS I) and 2011 (CFAS II).

Age Group	CFAS I				CFAS II			
	Total	Deaths	Frailty		Total	Deaths	Frailty	
	N	N	Mean	Median (IQR)	N	N	Mean	Median (IQR)
Overall								
65-69	1981	83	0.12	0.07 (0.03, 0.17)	1939	52	0.12	0.07 (0.03, 0.17)
70-74	1776	110	0.14	0.10 (0.03, 0.20)	1873	75	0.15	0.10 (0.07, 0.23)
75-79	1725	195	0.17	0.13 (0.07, 0.27)	1624	96	0.19	0.17 (0.07, 0.27)
80-84	1308	221	0.23	0.20 (0.10, 0.33)	1278	160	0.23	0.20 (0.10, 0.33)
85+	845	210	0.3	0.30 (0.20, 0.40)	1048	260	0.31	0.33 (0.20, 0.43)
All ages	7635	819	0.18	0.13 (0.07, 0.27)	7762	643	0.19	0.17 (0.07, 0.30)
Men								
65-69	915	57	0.11	0.07 (0.03, 0.13)	968	29	0.11	0.07 (0.03, 0.13)
70-74	780	67	0.12	0.10 (0.03, 0.17)	902	47	0.14	0.10 (0.03, 0.20)
75-79	696	110	0.16	0.10 (0.07, 0.23)	758	52	0.16	0.13 (0.07, 0.23)
80-84	449	93	0.2	0.17 (0.10, 0.30)	542	74	0.21	0.17 (0.07, 0.30)
85+	205	59	0.26	0.27 (0.13, 0.37)	364	92	0.26	0.27 (0.16, 0.40)
All ages	3045	386	0.15	0.10 (0.03, 0.20)	3534	294	0.16	0.10 (0.07, 0.23)
Women								
65-69	1066	26	0.13	0.10 (0.03, 0.17)	971	23	0.12	0.07 (0.03, 0.17)
70-74	996	43	0.15	0.10 (0.03, 0.23)	971	28	0.17	0.13 (0.06, 0.24)
75-79	1029	85	0.2	0.17 (0.07, 0.27)	866	44	0.21	0.17 (0.10, 0.30)
80-84	859	128	0.25	0.23 (0.13, 0.36)	736	86	0.26	0.23 (0.13, 0.37)
85+	640	151	0.31	0.33 (0.20, 0.40)	684	168	0.33	0.33 (0.23, 0.43)
All ages	4590	433	0.2	0.17 (0.07, 0.30)	4228	349	0.21	0.20 (0.07, 0.33)

Appendix 5: Predicted frailty index in a model adjusting for age, study and gender.



Appendix 6: The relationship between frailty and mortality for different frailty index (FI) scores

Frailty Index (FI)	Effect of a 0.1 increase in FI		Effect compared to FI=0	
	Ref FI	Odds Ratio (95%CI)	Ref FI	Odds Ratio (95%CI)
Model A^a				
0.1	0	2.08 (1.82, 2.33)	0	2.08 (1.82, 2.33)
0.2	0.1	1.96 (1.80, 2.11)	0	4.06 (3.26, 4.87)
0.3	0.2	1.84 (1.76, 1.92)	0	7.48 (5.75, 9.22)
0.4	0.3	1.74 (1.65, 1.83)	0	12.99 (9.99, 15.99)
0.5	0.4	1.64 (1.49, 1.78)	0	21.24 (16.60, 25.88)
0.6	0.5	1.54 (1.33, 1.75)	0	32.72 (24.65, 40.79)
0.7	0.6	1.45 (1.18, 1.72)	0	47.49 (30.26, 64.72)
Model B^b				
0.1	0	1.62 (1.41, 1.84)	0	1.62 (1.41, 1.84)
0.2	0.1	1.62 (1.48, 1.76)	0	2.63 (2.06, 3.20)
0.3	0.2	1.61 (1.54, 1.69)	0	4.25 (3.17, 5.32)
0.4	0.3	1.61 (1.52, 1.70)	0	6.84 (5.09, 8.59)
0.5	0.4	1.61 (1.45, 1.76)	0	10.97 (8.33, 13.62)
0.6	0.5	1.60 (1.37, 1.83)	0	17.57 (12.91, 22.24)
0.7	0.6	1.60 (1.29, 1.91)	0	28.05 (17.38, 38.73)
Final model^c				
0.1	0	1.64 (1.43, 1.86)	0	1.64 (1.43, 1.86)
0.2	0.1	1.63 (1.49, 1.77)	0	2.68 (2.10, 3.26)
0.3	0.2	1.62 (1.54, 1.70)	0	4.34 (3.23, 5.45)
0.4	0.3	1.61 (1.52, 1.70)	0	6.98 (5.19, 8.77)
0.5	0.4	1.60 (1.44, 1.75)	0	11.14 (8.42, 13.85)
0.6	0.5	1.58 (1.36, 1.81)	0	17.64 (12.92, 22.36)
0.7	0.6	1.57 (1.27, 1.88)	0	27.74 (17.17, 38.31)

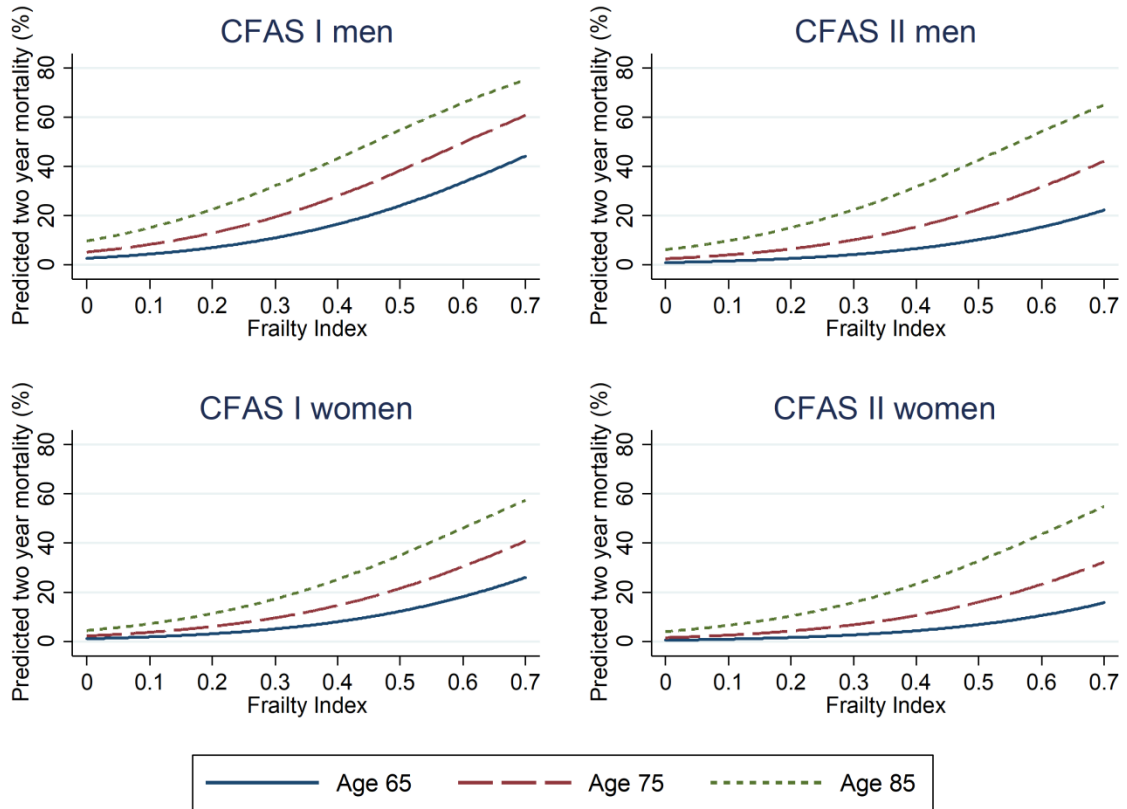
^a Model A: Frailty and Cohort change (study)

^b Model B: Frailty and Cohort change adjusted for sex and age differences

^cFinal model: Frailty and Cohort change adjusted for sex and age differences, and interactions between cohort change and sex and cohort and age

Note: Odds ratios and corresponding 95%Confidence Intervals are denoted for each comparison. All models were adjusted for the non-linear effect of frailty.

Appendix 7- Predicted mortality (%) by frailty for ages 65 (A), 75 (B), and 85 (C) shown for CFAS I men, CFAS II men, CFAS I women, and CFAS II women. The predicted lines were obtained from the final model which includes the study interactions by age and gender



Appendix 8- Predicted probabilities (as a percentage) of two year mortality for different numbers of deficits present, by age and sex.

Frailty	Predicted probability of 2-year mortality as a percentage (%)												
	Age	Men						Women					
		CFAS I			CFAS II			CFAS I			CFAS II		
	65	75	85	65	75	85	65	75	85	65	75	85	
None	2.8	5.3	9.9	1.0	2.6	6.3	1.3	2.4	4.6	0.7	1.7	4.2	
1 item	3.3	6.2	11.4	1.2	3.0	7.3	1.5	2.9	5.4	0.8	2.0	4.9	
2 items	3.8	7.2	13.2	1.4	3.5	8.5	1.7	3.4	6.3	0.9	2.3	5.8	
3 items	4.5	8.4	15.2	1.7	4.2	9.9	2.1	3.9	7.4	1.1	2.8	6.7	
4 items	5.3	9.8	17.5	2.0	4.9	11.5	2.4	4.6	8.6	1.3	3.2	7.8	
5 items	6.1	11.3	19.9	2.3	5.7	13.3	2.8	5.4	10.0	1.5	3.8	9.1	
6 items	7.1	13.0	22.7	2.7	6.6	15.2	3.3	6.3	11.5	1.8	4.4	10.5	
7 items	8.3	15.0	25.6	3.2	7.7	17.4	3.9	7.3	13.3	2.1	5.2	12.1	
8 items	9.6	17.2	28.8	3.7	8.9	19.9	4.5	8.4	15.2	2.5	6.0	14.0	
9 items	11.1	19.5	32.2	4.6	10.3	22.4	5.2	9.7	17.4	2.9	7.0	16.0	
10 items	12.7	22.2	35.7	5.0	11.8	25.4	6.1	11.2	19.8	3.3	8.1	18.3	
11 items	14.6	25.0	39.4	5.8	13.6	28.5	7.1	12.9	22.5	3.9	9.3	20.7	
12 items	16.7	28.1	43.2	6.8	15.5	31.9	8.2	14.8	25.3	4.8	10.8	23.4	
13 items	19.0	31.4	47.1	8.3	17.7	35.4	9.4	16.9	28.4	5.6	12.4	26.4	
14 items	21.5	34.8	51.0	9.6	20.1	39.0	10.8	19.2	31.6	6.5	14.1	29.5	
15 items	24.2	38.4	54.8	10.4	22.7	42.7	12.4	21.6	35.1	7.5	16.1	32.8	
16 items	27.1	42.1	58.5	12.6	25.5	46.6	14.1	24.4	38.7	8.1	18.4	36.3	
17 items	30.3	45.9	62.4	14.4	28.6	50.5	16.4	27.4	42.4	9.9	22.1	39.9	
18 items	33.6	49.7	65.7	16.4	31.7	54.0	18.3	30.5	46.1	11.4	24.8	43.8	
19 items	37.1	53.5	69.2	18.6	37.0	60.1	20.7	33.8	49.9	13.0	27.7	47.2	
20 items	40.6	57.2	72.7	21.0	40.5	63.6	23.3	37.3	53.7	14.8	30.9	51.6	

Appendix 9-AUC values for the prediction of death up to two years shown separately for CFAS I and II

MODEL	CFAS I	CFAS II
Age+Sex	0.71	0.76
Frailty	0.72	0.77
Frailty+Sex	0.73	0.77
Frailty+Age	0.75	0.80
Frailty+Sex+Age	0.76	0.81

Note: The models that included frailty as a covariate also included the non-linear effect of frailty

Appendix 10- Sensitivity analysis: (a) survival analysis and (b) removal of 3 readily diagnosed items

	Adjusted model			Stratified analysis					
	Coefficient [95% CI]			CFAS I			CFAS II		
	Coefficient [95% CI]			Coefficient [95% CI]			Coefficient [95% CI]		
(a) Cox regression									
Frailty Index	5.22	[3.79,	6.64]	4.44	[2.62,	6.26]	5.91	[3.74,	8.08]
Frailty Index squared	-1.42	[-3.68,	0.84]	-0.64	[-3.71,	2.43]	-2.18	[-5.47,	1.11]
Study	-3.03	[-4.20,	-1.87]						
Sex	-0.73	[-0.87,	-0.58]	-0.71	[-0.86,	-0.57]	-0.39	[-0.56,	-0.22]
Age	0.06	[0.05,	0.07]	0.06	[0.05,	0.07]	0.09	[0.07,	0.10]
Study by sex interaction	0.35	[0.13,	0.57]						
Study by age interaction	0.03	[0.02,	0.04]						
(b) removing 3 items: hypertension, thyroid problems and diabetes									
Frailty Index	4.67	[3.22,	6.13]	3.71	[1.91,	5.52]	5.41	[3.24,	7.59]
Frailty Index squared	-0.19	[-2.54,	2.17]	0.80	[-2.19,	3.79]	-0.98	[-4.45,	2.49]
Study	-2.68	[-3.99,	-1.36]						
Sex	-0.79	[-0.96,	-0.63]	-0.77	[-0.93,	-0.61]	-0.42	[-0.61,	-0.23]
Age	0.06	[0.05,	0.07]	0.07	[0.06,	0.08]	0.09	[0.07,	0.10]
Study by sex interaction	0.38	[0.14,	0.63]						
Study by age interaction	0.03	[0.01,	0.04]						
(c) removing 2 items: cognitive impairment and depression									
Frailty Index	4.70	[3.17,	6.24]	4.23	[2.33,	6.12]	5.19	[2.84,	7.54]
Frailty Index squared	-0.32	[-2.83,	2.19]	0.11	[-3.15,	3.36]	-0.85	[-4.52,	2.82]
Study	-2.70	[-4.03,	-1.38]						
Sex	-0.79	[-0.95,	-0.63]	-0.78	[-0.94,	-0.61]	-0.41	[-0.60,	-0.22]
Age	0.07	[0.06,	0.08]	0.07	[0.06,	0.08]	0.09	[0.08,	0.11]
Study by sex interaction	0.38	[0.14,	0.63]						
Study by age interaction	0.03	[0.01,	0.04]						

(a) Survival analysis and was used as a sensitivity analysis. The coefficient (β) for each covariate from the Cox regression model and its 95% Confidence Interval are shown. The exponential of these coefficients ($\exp(\beta)$) correspond to the hazard ratio(HR) of the covariate's effect. Negative coefficients will result to HRs between 0 and 1, showing a protective effect against mortality. Positive coefficients correspond to HRs over 1, showing greater risk of death.

(b) Another sensitivity analysis included the removal of 3 items from the frailty index which are now more readily diagnosed (hypertension, thyroid problems and diabetes). The coefficients and 95% CIs shown are from the logistic regression model. The exponential of those correspond to the Odds Ratios (ORs) of the covariate's effect.

(c) As a further sensitivity analysis, cognitive impairment and depression, which are markers of non-participation, were removed from the frailty index. Coefficients and 95% CIs are interpreted as in (b).

Frailty index was modelled as the proportion of deficits present. The reference category for study was CFAS I and the reference gender group was men. This analysis used non-response weights on the imputed data. Results are shown for the final (adjusted model) and for the models stratified by study.