

Supplementary Material

Outcome measurement

Nursing home admission and need for home care were measured using ICD-10 codes: a starting code of Z74 would mean that the patient received home care, while a Z59.3 code would represent an admission to a nursing home.

Confounder measurement

The information available up to the year of calculation on the start and end dates of smoking was used to determine which status had been predominant in the years of follow-up. For example, to know the smoking status of a patient in 2010, we looked at the patient's clinical records up to 2010 and calculated the duration of each possible status (i.e. non smoker, ex-smoker or smoker), if any available. The status that had been active for the longest time was assigned to the patient up to 2010. For example, if the person had been smoking for 25 years, until 2018, when they stopped smoking, their predominant status in 2010 would still be "smoker". The status was assigned yearly, considering possible changes over time.

The criteria for classifying patients according to alcohol intake (i.e. non-drinker, low-risk drinker, high-risk drinker) are presented in Table S1. At the discretion of the physician, patients were asked about their alcohol use at regular intervals during visits to primary care. The software converts the drinks self-reported by the patient into grams to automate the calculation of the category in which they belong.

	Men	Women
Risk 0: non-drinker	Non-drinker	Non-drinker
Risk 1: low-risk drinker	<280g of alcohol per week	<170g of alcohol per week
Risk 2: high-risk drinker	<280g of alcohol per week BUT - is younger than 16 years old - works with dangerous machinery - is taking any drug that interfere with alcohol	<170g of alcohol per week BUT - is pregnant - is younger than 16 years old - works with dangerous machinery - is taking any drug that interfere with alcohol
	≥280g of alcohol per week Drinks sporadically ≥ 60g of alcohol over a short period of time, at least once a month.	≥ 170g of alcohol per week Drinks sporadically ≥ 50g of alcohol over a short period of time, at least once a month.

Table S1: Classification criteria for alcohol intake according to the grams of alcohol ingested per week.

Imputation of confounders

Socioeconomic status (missing in 31·5% of participants) was imputed using *predictive mean matching*¹ and baseline year information. Smoking status and alcohol intake were missing in 6·0% and 50·5% of the registers, but all individuals but 3·99% and 14·83% had at least one register along follow-up, respectively. They were imputed using a two-level imputation (i.e. grouping the records coming from the same individual) through a logistic regression.² The imputation was carried out sequentially, imputing first the variables with

	2010 (N=943 671)	2011 (N=972 281)	2012 (N=993 549)	2013 (N=1 016 968)	2014 (N=1 031 330)	2015 (N=1 039 163)	2016 (N=1 047 876)	2017 (N=1 061 889)	2018 (N=1 071 339)	2019 (N=1 078 542)	Total (N=10 256 608)
Number of SNAC-K categories of chronic diseases	5 (4) [0-26]	5 (5) [0-26]	6 (4) [0-25]	6 (4) [0-27]	6 (5) [0-30]	7 (5) [0-23]	7 (5) [0-31]	7 (4) [0-29]	7 (5) [0-28]	7 (5) [0-29]	6 (5) [0-31]
Number of distinct diseases	8 (7) [0-86]	9 (8) [0-94]	10 (8) [0-103]	11 (9) [0-109]	12 (9) [0-105]	12 (9) [0-114]	13 (9) [0-115]	12 (9) [0-111]	13 (10) [0-95]	14 (10) [0-94]	12 (10) [0-115]
Multimorbidity	101 120	87 312	71 464	63 433	55 978	50 243	46 805	44 217	42 410	600 582	
Non-multimorbid	(10.7)	(9.0)	(7.2)	(6.2)	(5.4)	(4.8)	(4.5)	(4.4)	(4.1)	(5.9)	
Multimorbid	842 551	884 969	922 085	953 535	975 352	988 820	1 001 071	1 015 389	1 027 122	1 036 132	9 647 026
2-5 diseases	(89.3)	(91.0)	(92.8)	(93.8)	(94.6)	(95.2)	(95.5)	(95.6)	(95.9)	(96.1)	(94.1)
6-10 diseases	440 296	423 661	403 064	385 600	363 446	343 111	328 546	326 665	313 365	301 275	3 629 029
> 10 diseases	351 428	393 258	430 163	459 532	482 080	493 808	500 815	508 489	508 941	509 396	4 635 910
Deficit count (total)	508 27	68 050	88 858	108 405	129 826	151 901	171 710	182 235	204 816	225 461	1 382 087
Deficit count (diseases)	(5.4)	(7.0)	(8.9)	(10.7)	(12.0)	(14.6)	(16.1)	(17.5)	(19.1)	(20.3)	(13.5)
Deficit count (SSLD)	2 (2) [0-15]	2 (2) [0-15]	2 (3) [0-15]	2 (3) [0-15]	2 (3) [0-15]	2 (3) [0-15]	2 (3) [0-15]	2 (3) [0-15]	3 (3) [0-16]	3 (3) [0-16]	3 (3) [0-15]
Frailty	1 (2) [0-14]	2 (2) [0-14]	2 (2) [0-14]	2 (2) [0-14]	2 (2) [0-15]	2 (2) [0-15]	2 (2) [0-15]	2 (3) [0-16]	2 (3) [0-15]	2 (3) [0-16]	2 (2) [0-16]
Fit	580 818	554 758	524 258	509 679	490 551	481 580	468 174	471 437	461 157	453 896	4 996 308
Frail	(61.5)	(57.1)	(52.8)	(50.1)	(47.6)	(46.3)	(44.7)	(44.4)	(43.0)	(42.1)	(48.7)
Mild	362 853	417 523	469 291	507 289	540 779	557 583	579 702	590 452	610 182	624 646	5 260 300
Moderate	293 147	324 850	351 430	364 091	376 900	381 452	386 401	386 370	388 455	388 360	3 641 456
Severe	61 084	79 348	98 439	115 584	129 737	138 101	148 413	154 386	164 470	171 905	1 261 467
Multimorbidity & frailty	8 622	13 325	19 422	27 614	34 142	38 630	44 888	49 696	57 257	64 381	357 377
Non-multimorbid & Fit	100 414	86 648	70 876	62 904	55 568	50 056	46 555	46 259	44 024	42 227	605 531
Non-multimorbid & Frail	(10.6)	(8.9)	(7.1)	(6.2)	(5.4)	(4.8)	(4.4)	(4.4)	(4.1)	(3.9)	(5.9)
Multimorbid & Fit	706 (0-1)	664 (0-1)	588 (0-1)	529 (0-1)	410 (0-0)	287 (0-0)	250 (0-0)	241 (0-0)	193 (0-0)	183 (0-0)	4 051 (0.0)
Multimorbid & Frail	480 404	468 110	453 382	446 775	434 983	431 524	421 619	425 178	417 133	411 669	4 390 777
(Frail Multimorbid)	362 147	416 859	468 703	506 760	540 369	557 296	579 452	590 211	609 989	624 463	5 256 249
(Fit Multimorbid)	302 447	410 859	468 703	506 760	540 369	557 296	579 452	590 211	609 989	624 463	5 256 249
(Frail Multimorbid Frail)	(42.98)	(47.1)	(50.83)	(53.15)	(56.1)	(56.36)	(57.88)	(58.13)	(59.39)	(60.27)	(54.49)
(Fit Multimorbid Frail)	(48.44)	(46.110)	(453 382)	(446 775)	(434 983)	(431 524)	(421 619)	(425 178)	(417 133)	(411 669)	(4 390 777)
(Frail No-multimorbid)	706 (0-7)	664 (0-76)	588 (0-82)	529 (0-83)	410 (0-73)	287 (0-57)	250 (0-53)	241 (0-52)	193 (0-44)	183 (0-43)	4 051 (0.66)
(Fit No-multimorbid)	100 414	86 648	70 876	62 904	55 568	50 056	46 555	46 259	44 024	42 227	605 531 (9.34)
(Multimorbid Frail)	362 147	416 859	468 703	506 760	540 369	557 296	579 452	590 211	609 989	624 463	5 256 249 (9.92)
(No-multimorbid Frail)	706 (0-19)	664 (0-16)	588 (0-13)	529 (0-11)	410 (0-08)	287 (0-05)	250 (0-04)	241 (0-04)	193 (0-03)	183 (0-03)	4 051 (0.68)
(Multimorbid Fit)	480 404	468 110	453 382	446 775	434 983	431 524	421 619	425 178	417 133	411 669	4 390 777 (87.88)
(No-multimorbid Fit)	(82.71)	(84.58)	(86.48)	(87.66)	(88.67)	(89.61)	(90.66)	(90.19)	(90.45)	(90.7)	605 531 (12.12)

Table S2: Annual description of frailty and multimorbidity prevalence on the baseline year (2010) and during the follow-up (2010-2019).

Note: Categorical characteristics are described as n (%). Numeric characteristics are described as median (IQR) [min-max]. IQR: Interquartile range. Multimorbidity was defined as having ≥ 2 concurrent SNAC-K diagnostics. Frailty categories are defined according to the frailty score as follow: fit < 0.12 ; mild ≥ 0.12 , < 0.24 ; moderate ≥ 0.24 , < 0.36 ; severe ≥ 0.36 .

Note 2: In the section *Multimorbidity & Frailty*, the symbol & denotes the combination of both concepts (e.g. *Multimorbid & Fit* reports the proportion of individual who are simultaneously multimorbid and fit), while the symbol | denotes the conditional ratio (e.g. *Multimorbid | Fit* reports the proportion of people with multimorbidity between those that are fit).

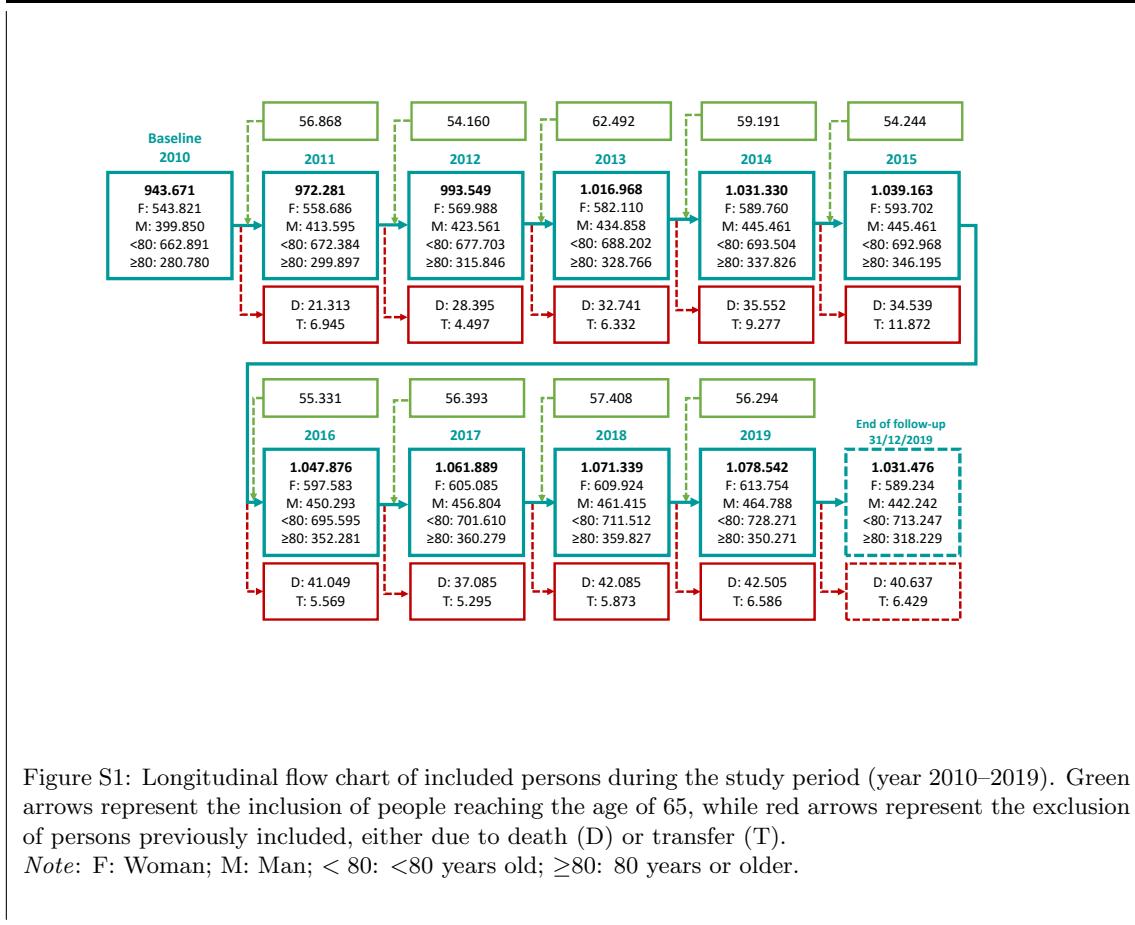
Variable	Level	Mortality									Nursing home admission									Need for home care									
		Deficit count			Deficit count, per deficit type			Frailty category			Deficit count			Deficit count, per deficit type			Frailty category			Deficit count			Deficit count, per deficit type			Frailty category			
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	
Deficit count (total)	-	1.1	1.10, 1.11	<0.001	-	-	-	-	-	-	1.4	1.40, 1.40	-	-	-	-	-	-	1.6	1.60, 1.60	<0.001	-	-	-	-	-	-		
Deficit count (diseases)	-	-	-	-	1.33	1.32, 1.35	<0.001	-	-	-	-	-	1.1	1.1, 1.1	-	-	-	-	-	-	0.99	0.99, 1	<0.001	-	-	-	-	-	-
Deficit count (SSLD)	-	-	-	-	1.03	1.03, 1.04	<0.001	-	-	-	-	-	1.9	1.90, 1.90	-	-	-	-	-	-	3.4	3.4, 3.4	<0.001	-	-	-	-	-	-
Mild	-	-	-	-	-	-	-	1.4	1.36, 1.45	<0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	19	18.97, 19.03	<0.001
Frailty	Moderate	-	-	-	-	-	-	2.24	2.15, 2.32	<0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	150	149.97, 150.03	-
Severe	-	-	-	-	-	-	-	2.77	2.64, 2.90	<0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	610	609.07, 610.03	-
Sex	Man	2.17	2.12, 2.21	-	2.13	2.09, 2.18	<0.001	2.15	2.11, 2.19	<0.001	0.92	0.91, 0.93	0.89	0.88, 0.90	0.91	0.90, 0.92	1.2	1.19, 1.21	<0.001	0.95	0.94, 0.96	<0.001	1.1	1.09, 1.11	<0.001	-	-	-	
Age	-	1.09	1.09, 1.09	<0.001	1.09	1.09, 1.09	<0.001	1.09	1.09, 1.09	<0.001	1.1	1.10, 1.10	1.1	1.10, 1.10	1.1	1.10, 1.10	1.1	1.10, 1.10	<0.001	1.1	1.10, 1.10	0.02	1.1	1.10, 1.10	<0.001	-	-	-	
Depprivation index	2	1.14	1.10, 1.18	<0.001	1.14	1.10, 1.18	<0.001	1.14	1.10, 1.18	<0.001	0.75	0.74, 0.76	0.74	0.73, 0.75	0.74	0.73, 0.75	1	0.99, 1.01	0.14	1	0.99, 1.01	<0.001	1	0.99, 1.01	0.2	-	-	-	
5 (More deprived)	3	1.23	1.19, 1.26	<0.001	1.24	1.20, 1.27	<0.001	1.22	1.18, 1.26	<0.001	0.75	0.74, 0.76	0.75	0.74, 0.76	0.74	0.73, 0.75	1.1	1.09, 1.11	<0.001	1.1	1.09, 1.11	<0.001	1.1	1.09, 1.11	<0.001	-	-	-	
Alcohol consumption	4	1.24	1.20, 1.28	<0.001	1.25	1.21, 1.29	<0.001	1.24	1.20, 1.28	<0.001	0.59	0.58, 0.60	0.6	0.59, 0.61	0.59	0.58, 0.60	1.1	1.09, 1.11	<0.001	1.2	1.19, 1.21	<0.001	1.1	1.09, 1.11	<0.001	-	-	-	
Smoking status	5 (More deprived)	1.31	1.25, 1.37	<0.001	1.32	1.25, 1.38	<0.001	1.31	1.25, 1.37	<0.001	0.48	0.47, 0.62	0.6	0.58, 0.62	0.6	0.58, 0.62	1.2	1.18, 1.22	<0.001	1.2	1.19, 1.21	<0.001	1.2	1.18, 1.22	<0.001	-	-	-	
Low-risk drinker	0.55	0.54, 0.57	<0.001	0.57	0.55, 0.58	<0.001	0.55	0.54, 0.57	<0.001	1.1	1.09, 1.11	1.1	1.09, 1.11	1	0.99, 1.01	0.59	0.58, 0.60	<0.001	0.71	0.70, 0.72	<0.001	0.58	0.57, 0.59	<0.001	-	-	-		
High-risk drinker	0.9	0.81, 0.99	0.03	0.91	0.82, 1.00	0.05	0.9	0.81, 0.99	0.03	1.3	1.26, 1.34	1.3	1.26, 1.34	1.3	1.26, 1.33	0.83	0.77, 0.89	<0.001	0.85	0.79, 0.91	0.003	0.84	0.79, 0.90	0.002	-	-	-		
Non-smoker	1.27	1.25, 1.30	<0.001	1.27	1.24, 1.30	<0.001	1.28	1.26, 1.31	<0.001	0.91	0.90, 0.92	0.91	0.90, 0.92	0.94	0.93, 0.95	0.97	0.96, 0.98	0.02	1	0.99, 1.01	0.6	1	0.99, 1.01	0.65	-	-	-		
Smoker	1.82	1.76, 1.89	<0.001	1.79	1.73, 1.86	<0.001	1.82	1.76, 1.89	<0.001	1.3	1.28, 1.32	1.2	1.18, 1.22	1.3	1.28, 1.32	1.4	1.38, 1.42	<0.001	1.1	1.09, 1.12	<0.001	1.4	1.38, 1.42	<0.001	-	-	-		
Nursing home admission	Yes	2.26	2.18, 2.33	<0.001	2.03	1.96, 2.09	<0.001	2.31	2.24, 2.38	<0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Need for home care	Yes	3.35	3.26, 3.43	<0.001	2.27	2.20, 2.34	<0.001	4	3.42, 3.59	<0.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AIC		1 050 389	1 048 250		1 050 680	1 375 684		1 358 164	1 377 487		2 271 520	2 271 520		2 140 875	2 279 921														

Table S3: Association between frailty and the risk of all-cause mortality, nursing home admission, and needing home care using only complete cases.

Note: Three models are reported for each outcome, one for each frailty measure: sum of all deficits, sum of deficits, per deficit type, and frailty category. Models for nursing home admission and needing home care accounted the competing risk of death. Reference groups were the following: woman, for sex; non-drinker, for alcohol consumption; non-smoker for smoking status; least deprived, for deprivation index; and fit, for frailty. p-values for the nursing home admission models are not reported as all of them were < 0.001. HR: Hazard Ratio, CI: Confidence Interval, AIC: Akaike's Information Criterion.

Note 2: Data from 1 041 678 distinct individuals was used for fitting the models with complete cases. Individuals were followed-up for 7.29 ± 2.61 months for the mortality model, 8.74 ± 3.12 for the nursing home admission model, and 8.76 ± 2.12 for the need for home care model.

Supplementary figures



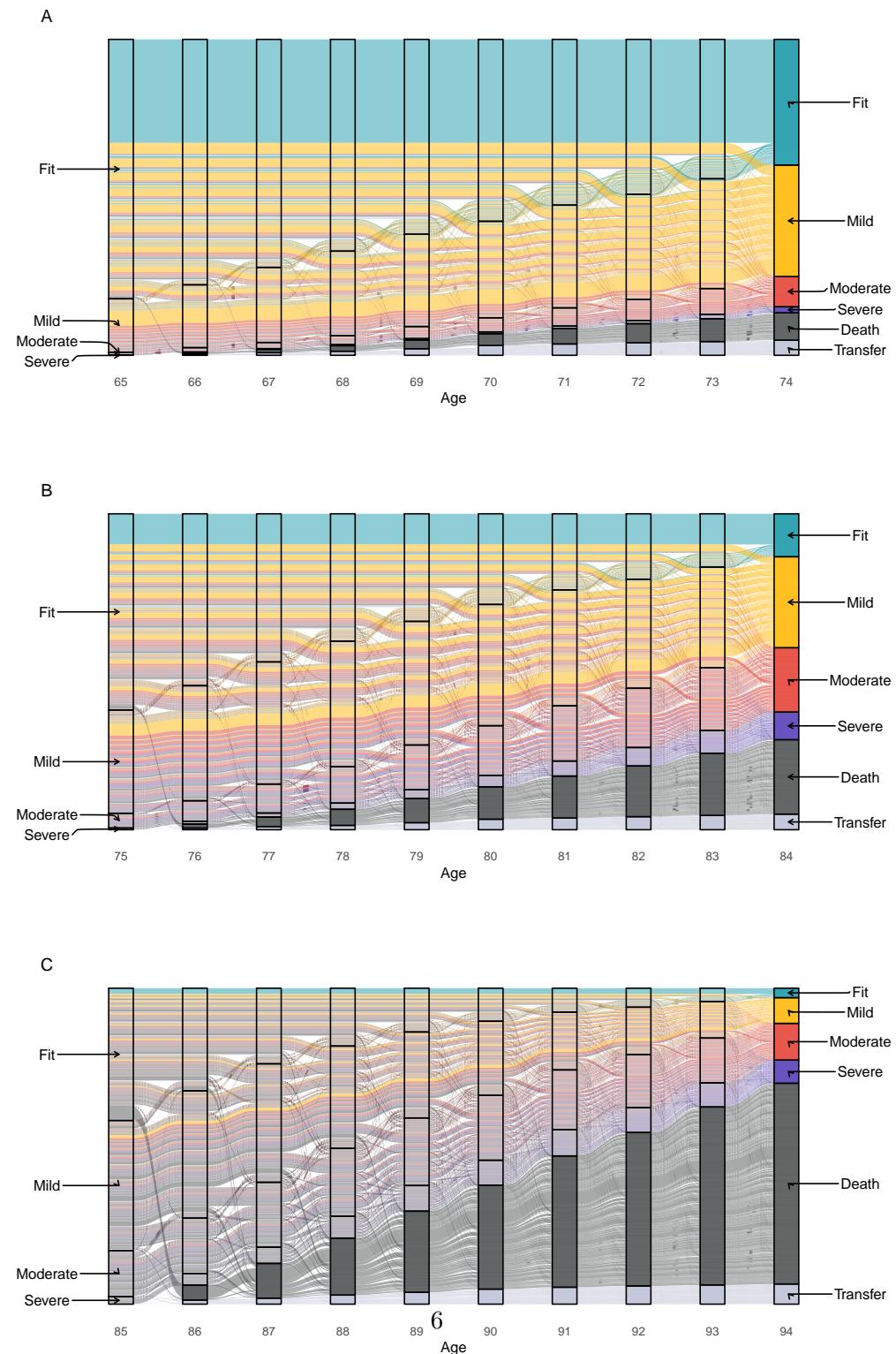
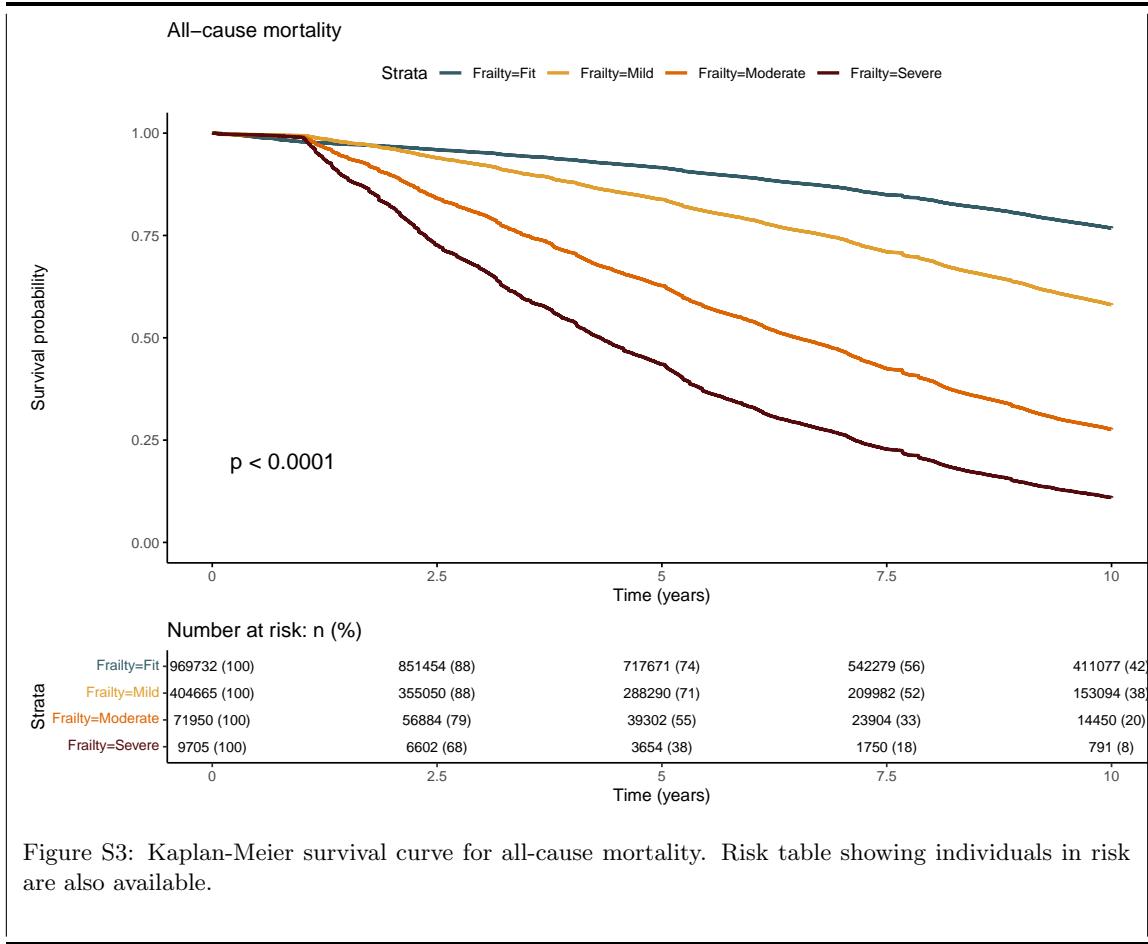
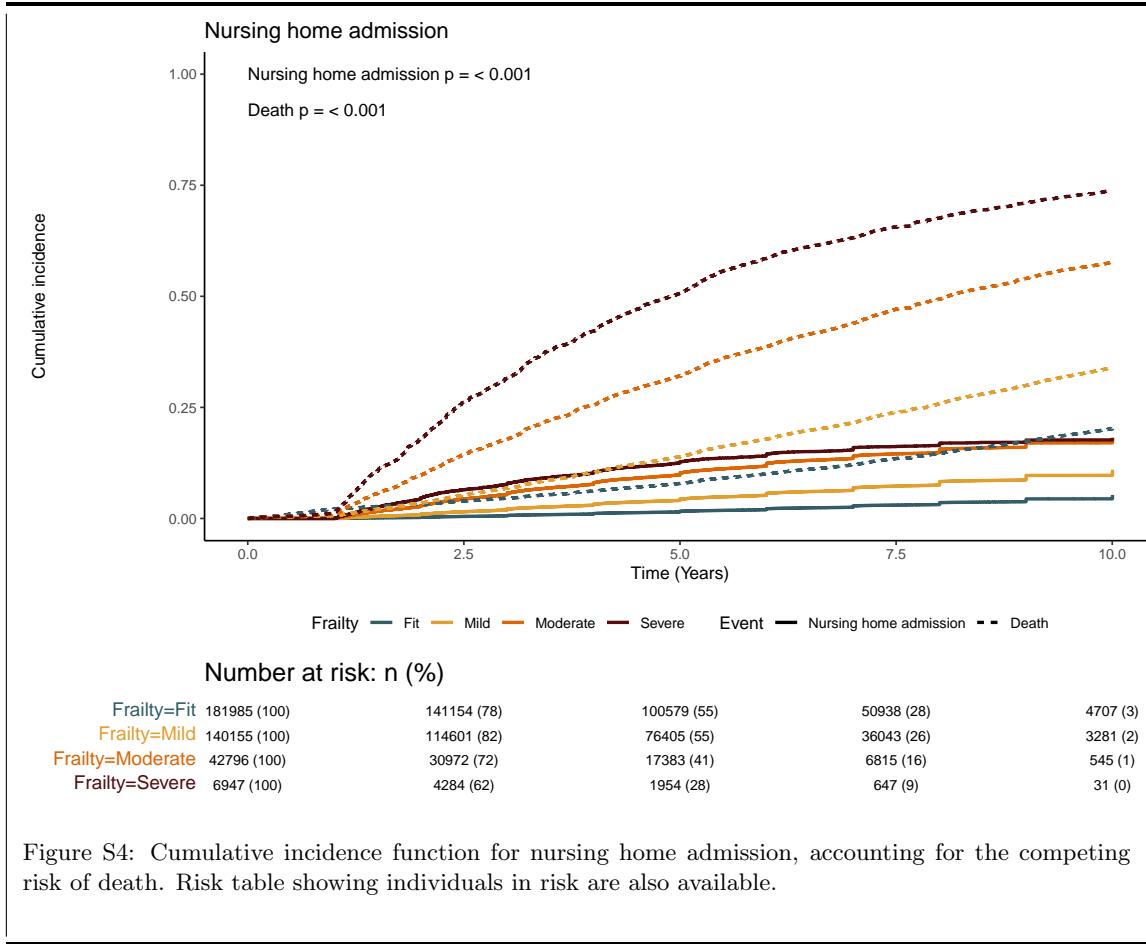
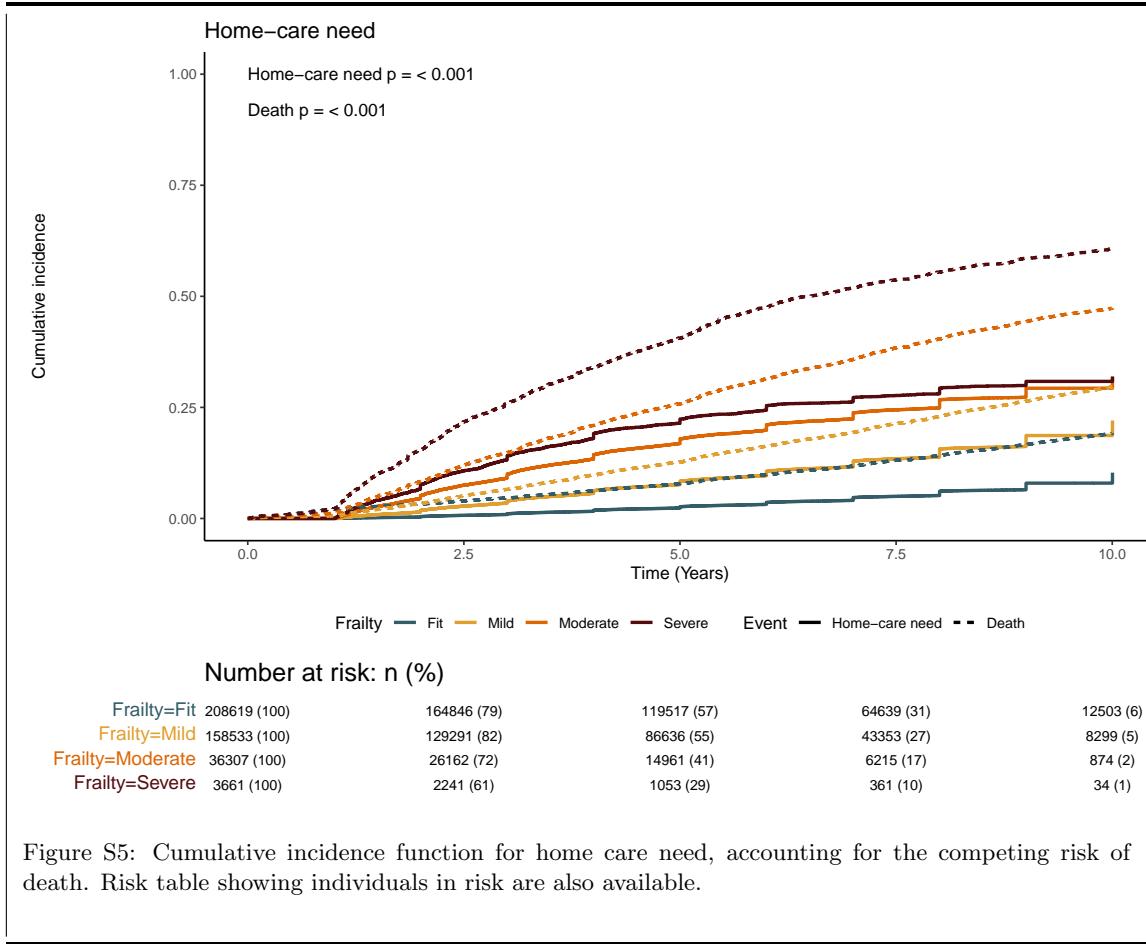


Figure S2: dynamics of frailty in 20.000 random individuals which follow-up started with 65 (Figure S2A), 75 (Figure S2B), and 85 (Figure S2C). The flows are coloured according to the final frailty situation.







References for Supplementary Material

- ¹ Little RJA. Missing-Data Adjustments in Large Surveys. *Journal of Business & Economic Statistics*. 1988 Jul;6(3):287. Available from: <https://doi.org/10.2307/1391878>.
- ² Jolani S, Debray TPA, Koffijberg H, van Buuren S, Moons KGM. Imputation of systematically missing predictors in an individual participant data meta-analysis: a generalized approach using MICE. *Statistics in Medicine*. 2015;34(11):1841-63. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/sim.6451>.