Supplementary Table 1. Health variables used for construction of cumulative frailty index

Sl.no	Variable	Coding
1	Help bathing	Yes = 1, No = 0
2	Help dressing	Yes = 1, No = 0
3	Help getting in/out of chair	Yes = 1, No = 0
4	Help walking around house	Yes = 1, No = 0
5	Help eating	Yes = 1, No = 0
6	Help grooming	Yes = 1, No = 0
7	Help using toilet	Yes = 1, No = 0
8	Help up/down stairs	Yes = 1, No = 0
9	Help lifting 10 lbs	Yes = 1, No = 0
10	Help shopping	Yes = 1, No = 0
11	Help with housework	Yes = 1, No = 0
12	Help with meal preparations	Yes = 1, No = 0
13	Help taking medication	Yes = 1, No = 0
14	Help with finances	Yes = 1, No = 0
15	Lost more than 10 lbs in last year	Yes = 1, No = 0
16	Self rating of health	Poor = 1, Fair = 0.75, Good = 0.5, V. Good = 0.25, Excellent = 0
17	How health has changed in last year	Worse = 1, Better/Same = 0
18	Hospitalized/ER visits	Yes = 1, No = 0
19	Cut down on usual activity (in last month)	Yes = 1, No = 0
20	Walk outside	<3 days = 1, ≤ 3 days = 0
21	Feel everything is an effort	Most of time = 1, Some time = 0.5, Rarely = 0
22	Feel depressed	Most of time = 1, Some time = 0.5, Rarely = 0
23	Feel happy	Most of time = 0, Some time = 0.5, Rarely = 1
24	Health interfered with social activities	Not at all - Slightly = 0, Moderately - Extremely = 1
25	Have trouble getting going	Most of time = 1, Some time = 0.5, Rarely = 0
26	Moderate activity affected	Yes = 1, No = 0
27	High blood pressure	Yes = 1, No = 0
28	Heart attack	Yes = 1, No = 0
29	CHF	Yes = 1, No = 0
30	Stroke	Yes = 1, No = 0
31	Cancer	Yes = 1, No = 0
32	Diabetes	Yes = 1, No = 0
33	Arthritis	Yes = 1, No = 0
34	Chronic lung disease	Yes = 1, No = 0
35	Cognitive test: Blessed	<2=0: 2-3=0.25: 4-7=0.50: >7 =1
36	Peak flow	Men=<340 liters/min; Women=<310 liters/min
37	BMI	1 if BMI <18.5 or >=30

38	Grip strength	Men BMI=<24, GS=<29 : Men BMI 24.1-28, GS=<30:Men BMI>28, GS=<32: Women BMI=<23, GS=<17:Women BMI 23.1-26, GS=<17.3:Women BMI 26.1-29,GS=<18: Women BMI >29, GS=<21
39	Falls	Yes = 1, No = 0
40	Memory changes	Yes = 1, No = 0
41	History of Parkinson's disease	Yes = 1, No = 0

Supplementary table 2. Post hoc analysis of association of frailty trajectories with mortality. Model adjusted for cohort status and covariates presented below.

Variables	**Hazard ratio (95% confidence intervals)**
Frailty trajectories	
Relatively stable	Reference
Mild frail	2.88 (1.38 - 6.04)
Moderate frail	2.62 (1.08 – 6.36)
Severely frail	5.47 (1.82 – 16.45)
Age, years	1.08 (1.04 – 1.12)
Male sex	2.24 (1.51 – 3.32)
Education, years	0.99 (0.93 – 1.06)
Frailty Index score	1.56 (0.04 – 55.71)
Comorbidities score	1.02 (0.82 – 1.27)
Walking speed, cm/s	0.99 (0.98 – 1.00)
Body mass index, kg/m^2	0.96 (0.92 – 1.01)
Free recall score	1.00 (0.96 – 1.04)
DSST score*	0.81 (0.66 – 1.00)

***DSST:** Digit symbol substitution test. Scores were standardized as timing of administration varied between LonGenity (90 seconds) and Einstein Aging study (60 seconds).

Supplementary Table 3. Proteomics and frailty trajectories. Eleven significant SOMAmer reagent targets associated with frailty trajectories; linear regression comparing the combined frail trajectory groups versus the relatively stable trajectory group as reference.

SomaId	Target	Target Full Name	UniProt	Estimate	Std Error	p value
SL001774	H-FABP	Fatty acid-binding protein, heart	P05413	0·148	0·027	6·08E-08
SL008782	CSPG3	Neurocan core protein	O14594	-0·127	0·025	6·73E-07
SL000498	Leptin	Leptin	P41159	0·267	0·054	8·62E-07
SL018710	CA2D3	Voltage-dependent calcium channel subunit alpha-2/delta-3	Q8IZS8	-0·094	0·020	2·89E-06
SL008968	DNER	Delta and Notch-like epidermal growth factor-related receptor	Q8NFT8	-0·094	0·020	3·39E-06
SL005086	FABPA	Fatty acid-binding protein, adipocyte	P15090	0·126	0·027	3·85E-06
SL002644	ERBB1	Epidermal growth factor receptor	P00533	-0·053	0·011	3·9E-06
SL011048	ANTR2	Anthrax toxin receptor 2	P58335	-0·102	0·022	6·15E-06

SL010377	OMGP	Oligodendrocyte-myelin glycoprotein	P23515	-0·162	0·036	7·78E-06
SL004855	contactin-1	Contactin-1	Q12860	-0·066	0·015	7·88E-06
SL000070	Glypican 3	Glypican-3	P51654	-0·101	0·023	9·08E-06

log(SOMAmer) ~ Trajectory Group + Age + Gender + OPEL-OPUS status