Supplementary Appendix – Contents

Association of Intrinsic Capacity with Mortality and Incidence of Cardiovascular Disease: Prospective Study in UK Biobank

Table S1. Descriptive cross-sectional analysis of baseline variables and intrinsic capacity scoring.

Characteristic	0 Factors (better IC)		1 Factor		2 Factors		3 Factors		+ 4 Factors (deficit IC)		P-value
	Count	%	Count	%	Count	%	Count	%	Count	%	
Sex											
Male	82361	55.16	84623	52.65	46131	53.36	18593	56.37	8008	58.68	<0.001
Female	66961	44.84	76096	47.35	40327	46.64	14390	43.63	5640	41.32	
Age, years (mean SD)	149322	57.04 (8.20)	160719	58.57 (8.05)	86458	59.50 (7.88)	32983	60.08 (7.70)	13648	60.57 (7.40)	<0.001
Sex											
37-56 years	68888	46.13	61147	38.05	28973	33.51	10067	30.52	3774	27.65	
56-65 years	27131	18.17	37728	23.47	23259	26.90	9662	29.29	4171	30.56	<0.001
+65 years	53303	35.70	61844	38.48	34226	39.59	13254	40.18	5703	41.79	
Ethnicity											
White	144046	96.47	152849	95.10	81009	93.70	30243	91.69	12238	89.67	
Black	527	0.35	978	0.61	718	0.83	343	1.04	157	1.15	
Chinese	426	0.29	457	0.28	281	0.33	99	0.30	26	0.19	<0.001
Mixed	756	0.51	973	0.61	529	0.61	211	0.64	123	0.90	
Other ethnic group	3204	2.15	5021	3.12	3635	4.20	1934	5.86	1025	7.51	
Missing	363	0.24	441	0.27	286	0.33	153	0.46	79	0.58	
Socioeconomic status (Townsend score)											
Quartile 1 (least dep)	43287	28.99	41931	26.09	20052	23.19	6324	19.17	1922	14.08	
Quartile 2	40146	26.89	41674	25.93	20893	24.17	7101	21.53	2456	18.00	
Quartile 3	36876	24.70	40645	25.29	21849	25.27	8306	25.18	3287	24.08	<0.001
Quartile 4 (most dep)	28849	19.32	36276	22.57	23537	27.22	11209	33.98	5962	43.68	
Missing	164	0.11	193	0.12	127	0.15	43	0.13	21	0.15	
Alcohol intake											
Never	7776	5.21	10909	6.79	7831	9.06	4393	13.32	2693	19.73	
Special occasions only	12672	8.49	16605	10.33	11287	13.05	5529	16.76	3002	22.00	
One to three times a month	15534	10.40	17578	10.94	10211	11.81	4085	12.39	1688	12.37	
Three or four times a week	39924	26.74	38663	24.06	18207	21.06	5613	17.02	1642	12.03	<0.001
Once or twice a week	39563	26.50	42004	26.14	22266	25.75	8064	24.45	2943	21.56	
Daily or almost daily	33815	22.65	34875	21.70	16596	19.20	5251	15.92	1656	12.13	
Missing	38	0.03	85	0.05	60	0.07	48	0.15	24	0.18	
Cooked vegetable intake											
Mean (SD)	148402	2.68 (1.78)	159358	2.73 (1.89)	85410	2.77 (2.04)	32450	2.77 (2.17)	13333	2.74 (2.29)	<0.001
Salad vegetable intake											

Mean (SD)	148330	2.16 (2.07)	159227	2.17 (2.14)	85397	2.18 (2.25)	32410	2.15 (2.29)	13331	2.11 (2.39)	<0.001
Fresh fruit vegetable intake											
Mean SD	149055	2.20 (1.52)	160354	2.22 (1.58)	86150	2.25 (1.72)	32795	2.24 (1.76)	13536	2.26 (1.96)	<0.001
Dried fruit vegetable intake											
Mean (SD)	148386	0.82 (1.67)	159409	0.81 (1.73)	85559	0.81 (1.88)	32515	0.78 (1.74)	13425	0.76 (1.98)	<0.001
Smoking status											
Never	87347	58.50	87666	54.55	44861	51.89	16310	49.45	6219	45.57	<0.001
Current	13436	9.00	15798	9.83	9741	11.27	4332	13.13	2360	17.29	
Previous	48248	32.31	56794	35.34	31528	36.47	12168	36.89	4990	36.56	
Missing	291	0.19	461	0.29	328	0.38	173	0.52	79	0.58	
Physical activity											
No	141041	94.45	148114	92.16	75726	87.59	26120	79.19	8727	63.94	<0.001
Yes	8254	5.53	12527	7.79	10652	12.32	6789	20.58	4846	35.51	
Missing	27	0.02	78	0.05	80	0.09	74	0.22	75	0.55	
Time spent using TV											
No	80255	53.75	77099	47.97	37012	42.81	12048	36.53	3951	28.95	<0.001
Yes	68576	45.92	82799	51.52	48798	56.44	20534	62.26	9366	68.63	
Missing	491	0.33	821	0.51	648	0.75	401	1.22	331	2.43	
Time spent using CPU											
No	135917	91.02	143928	89.55	76415	88.38	28659	86.89	11629	85.21	<0.001
Yes	12850	8.61	15891	9.89	9258	10.71	3895	11.81	1714	12.56	
Missing	555	0.37	900	0.56	785	0.91	429	1.30	305	2.23	
BMI Mean (SD)	149322	26.37 (4.11)	160719	27.23 (4.47)	86458	28.17 (4.97)	32983	29.32 (5.66)	13648	30.68 (6.38)	<0.001

CPU, computer; TV, Television; BMI, body mass index; SD, standard deviation

Table S2. Intrinsic capacity domains and factors adapted from World Health Organization (WHO) and used in the Biobank study.

Domain	Factors	UK Biobank criteria	UK Biobank code
Psychological	Exhaustion	Self-reported: "Over the past two weeks, how often have you felt tired or had little energy?" (Response: more than half the days, nearly every day = 1 point; not at all, several days = 0 point)	2080
	Sleep duration	Self-reported: "About how many hours sleep do you get in every 24 hours? (Include naps)" (Response: short <7 h/d or long >9 h/d =1; healthy 7-9 h/d = 0 points)	1160
Sensory	Eye problems	Self-reported: non-cancer illness, self-reported considering eye/eyelid problem category (Response: yes, I am completely deaf = 1 point; no = 0 point)*	Data-Coding 6 (non-cancer Illness) Nodes: 1242, 1247, 1275, 1281, 1282, 1527, 1528, 1276, 1277, 1278, 1279, 1435, 1529, 1530, 1613
	Hearing difficulty	Self-reported: "Do you have any difficulty with your hearing?" (Response: yes, I am completely deaf = 1 point; no = 0 point)	2247
Vitality	Weight loss	Self-reported: "Compared with one year ago, has your weight changed?" (Response: yes - lost weight = 1 point; no - weight the same, yes - gain weight = 0 point)	2306
	Low grip strength	Measured grip strength (sex and body-mass index adjusted cut-offs taken from Fried and colleagues) **	31, 46, 47, 23104

		BMI by sex	Cut-off (kg) criterion for frailty	
		Men BMI ≤ 24 BMI 24.1–26 BMI 26.1–28 BMI > 28	 ≤ 29 ≤ 30 ≤ 30 ≤ 32	
		Women BMI ≤ 23 BMI 23.1–26 BMI 26.1–29 BMI > 29	 ≤ 17 ≤ 17.3 ≤ 18 ≤ 21	
Locomotor	Slow walking pace	Self-reported: "How would you describe your usual walking pace?" (Response: slow pace = 1 point; steady average pace or brisk pace = 0 point)	924	

* Approximation based on available variables in UK Biobank assessment centre data. Field 20002 encoded using Data-Coding 6 and selecting only codes related to eye/eyelid problems category.

** Definition used in original description by Fried and colleagues[i].

BMI, body mass index

Figure S1. Prevalence of IC scoring by number of long-term CVD conditions (LTC) in baseline sample (n=443 130 participants).
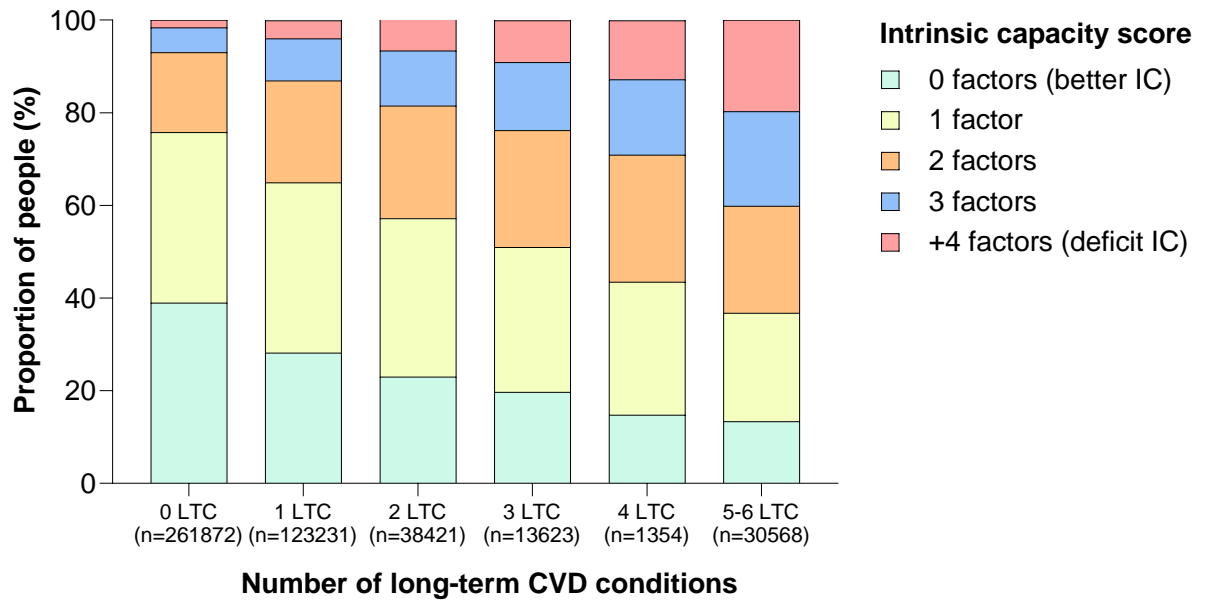
Figure S2. Prevalence of IC scoring and long-term CVD conditions (LTC) by full sample, sex and age categories (37–55, 55–65, and +65 years), in baseline sample (n=443 130 participants).
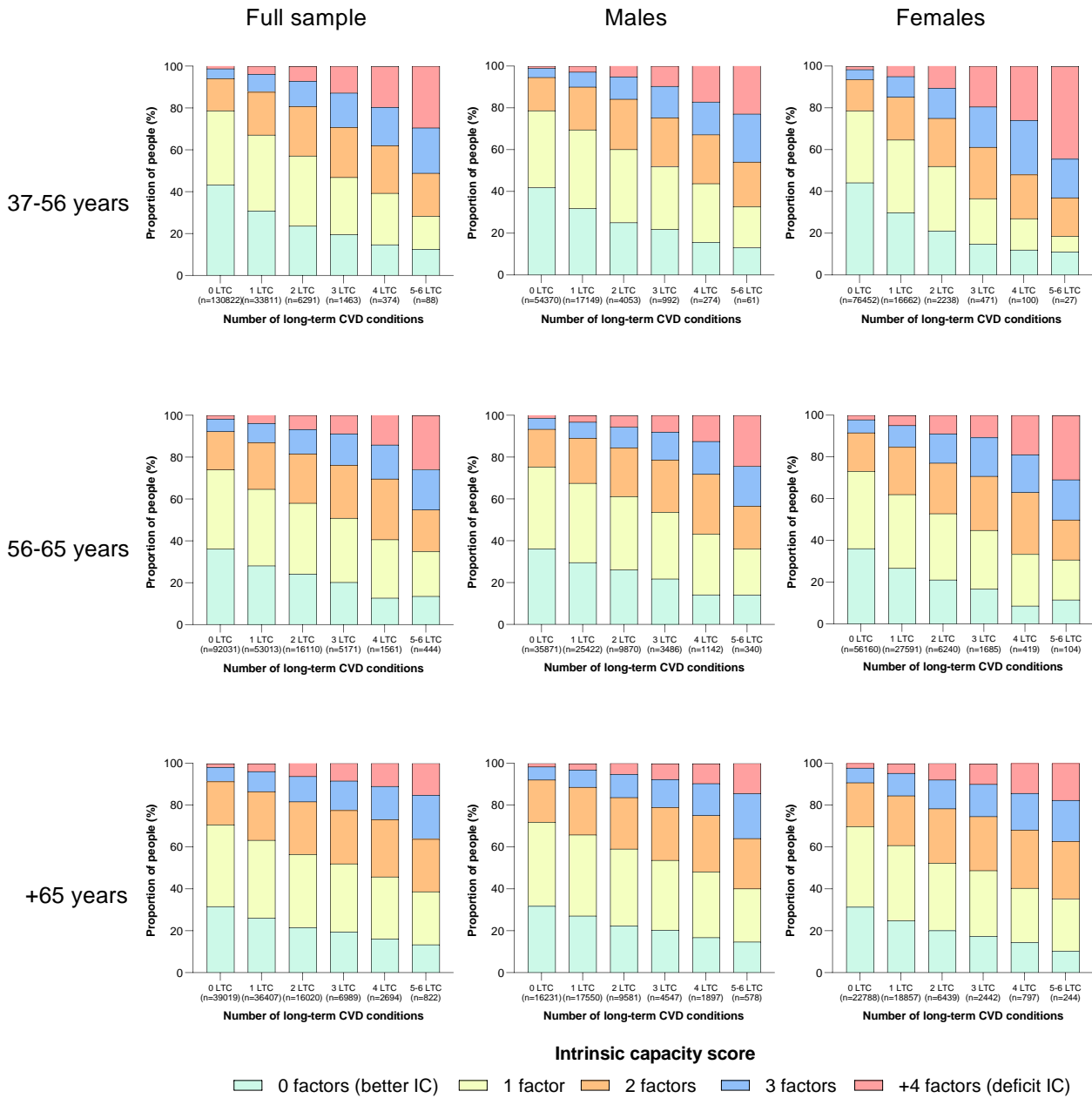
Table S3. Association of intrinsic capacity with individual incidence of long-term CVD conditions for males (n = 173 504): univariate and multivariate analysis model.

Morbidity	Affected*	1 factor (better IC)				2 factors				3 factors				+4 factors (deficit IC)				C-index
		Total	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	
Hypertension																			
Model 1	25395	146083	1.29	1.26	1.33	< 0.0001	1.60	1.54	1.65	< 0.0001	1.98	1.89	2.08	< 0.0001	2.78	2.59	2.98	< 0.0001	0.56
Model 2	24501	141854	1.19	1.15	1.23	< 0.0001	1.38	1.33	1.43	< 0.0001	1.65	1.57	1.73	< 0.0001	2.14	1.99	2.31	< 0.0001	0.66
Model 3	24193	140629	1.13	1.10	1.17	< 0.0001	1.25	1.20	1.29	< 0.0001	1.38	1.31	1.45	< 0.0001	1.65	1.53	1.78	< 0.0001	0.69
Stroke/TIA																			
Model 1	5787	198546	1.20	1.12	1.28	< 0.0001	1.37	1.27	1.47	< 0.0001	1.86	1.70	2.05	< 0.0001	2.20	1.93	2.51	< 0.0001	0.55
Model 2	5570	192531	1.07	1.00	1.14	0.0576	1.14	1.05	1.23	0.0011	1.48	1.34	1.63	< 0.0001	1.60	1.39	1.83	< 0.0001	0.67
Model 3	5497	190686	1.05	0.99	1.13	0.1210	1.11	1.02	1.20	0.0108	1.41	1.28	1.56	< 0.0001	1.48	1.28	1.70	< 0.0001	0.67
Per. Vascular																			
Model 1	3514	201615	1.33	1.21	1.46	< 0.0001	1.99	1.80	2.19	< 0.0001	2.80	2.49	3.15	< 0.0001	4.73	4.14	5.42	< 0.0001	0.61
Model 2	3354	195473	1.18	1.07	1.29	0.0007	1.63	1.47	1.80	< 0.0001	2.11	1.87	2.38	< 0.0001	3.20	2.78	3.69	< 0.0001	0.72
Model 3	3299	193586	1.15	1.04	1.26	0.0053	1.50	1.36	1.66	< 0.0001	1.80	1.59	2.04	< 0.0001	2.52	2.17	2.93	< 0.0001	0.75
Atrial fibrillation																			
Model 1	13499	197693	1.22	1.17	1.27	< 0.0001	1.50	1.43	1.58	< 0.0001	1.85	1.73	1.97	< 0.0001	2.54	2.34	2.75	< 0.0001	0.56
Model 2	13028	191682	1.09	1.04	1.14	0.0001	1.26	1.19	1.32	< 0.0001	1.47	1.38	1.57	< 0.0001	1.95	1.79	2.12	< 0.0001	0.70
Model 3	12870	189828	1.05	1.00	1.10	0.0321	1.16	1.10	1.22	< 0.0001	1.27	1.19	1.36	< 0.0001	1.56	1.43	1.71	< 0.0001	0.72
CHD																			
Model 1	10078	188189	1.28	1.21	1.34	< 0.0001	1.57	1.48	1.66	< 0.0001	1.94	1.80	2.09	< 0.0001	2.63	2.37	2.90	< 0.0001	0.56
Model 2	9731	182560	1.18	1.12	1.24	< 0.0001	1.38	1.30	1.46	< 0.0001	1.64	1.51	1.76	< 0.0001	2.08	1.87	2.31	< 0.0001	0.64
Model 3	9625	180863	1.15	1.09	1.21	< 0.0001	1.29	1.22	1.37	< 0.0001	1.46	1.35	1.58	< 0.0001	1.69	1.51	1.89	< 0.0001	0.65
Heart failure																			
Model 1	6986	201148	1.31	1.22	1.40	< 0.0001	1.93	1.80	2.07	< 0.0001	2.70	2.49	2.94	< 0.0001	4.82	4.38	5.30	< 0.0001	0.61
Model 2	6696	195025	1.14	1.07	1.22	0.0001	1.54	1.44	1.65	< 0.0001	1.97	1.81	2.15	< 0.0001	3.21	2.90	3.55	< 0.0001	0.72
Model 3	6587	193127	1.08	1.01	1.16	0.0179	1.36	1.26	1.46	< 0.0001	1.60	1.46	1.75	< 0.0001	2.25	2.02	2.50	< 0.0001	0.74

CHD, Cardiovascular heart disease. Model 1 was unadjusted. Model 2 was adjusted as for age, deprivation index, ethnicity, alcohol intake and dietary intakes. Model 3 (fully adjusted) was adjusted as in model 2 but also included lifestyle factors (smoking status, physical activity, time spent using TV/CPU), and BMI. The incremental effect of increasing number of IC factors was assessed by comparing the HRs for the presence of one, two, three, or four indicators, using the cero factors as the reference group. The number of missing data in model 1 to 3 are derived for the variables as: education, income, race, Townsend index, smoking status, alcohol consumption, BMI and sedentary behavior. * The values for the number of affected were based on complete cases.

Table S4. Association of intrinsic capacity with individual incidence of long-term CVD conditions for females (n =): univariate and multivariate analysis model.

Morbidity	Affected*	1 factor (better IC)				2 factors				3 factors				+4 factors (deficit IC)				C-index
		Total	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	
Hypertension																			
Model 1	23937	190277	1.42	1.37	1.47	< 0.0001	1.86	1.79	1.92	< 0.0001	2.49	2.38	2.60	< 0.0001	3.37	3.17	3.58	< 0.0001	0.59
Model 2	23260	186239	1.25	1.21	1.30	< 0.0001	1.50	1.45	1.56	< 0.0001	1.91	1.82	2.01	< 0.0001	2.43	2.28	2.59	< 0.0001	0.68
Model 3	22776	183934	1.18	1.14	1.22	< 0.0001	1.31	1.26	1.36	< 0.0001	1.52	1.44	1.59	< 0.0001	1.74	1.63	1.86	< 0.0001	0.71
Stroke/TIA																			
Model 1	4250	236202	1.33	1.23	1.44	< 0.0001	1.73	1.59	1.89	< 0.0001	2.12	1.90	2.36	< 0.0001	3.13	2.76	3.56	< 0.0001	0.58
Model 2	4112	230857	1.16	1.07	1.26	0.0004	1.39	1.27	1.52	< 0.0001	1.57	1.40	1.75	< 0.0001	2.23	1.95	2.55	< 0.0001	0.70
Model 3	4011	227654	1.14	1.05	1.24	0.0016	1.32	1.21	1.45	< 0.0001	1.42	1.27	1.60	< 0.0001	1.93	1.67	2.22	< 0.0001	0.70
Per. Vascular																			
Model 1	2723	238327	1.45	1.31	1.61	< 0.0001	1.91	1.71	2.14	< 0.0001	2.83	2.49	3.23	< 0.0001	4.69	4.05	5.42	< 0.0001	0.61
Model 2	2632	232912	1.30	1.17	1.44	< 0.0001	1.59	1.41	1.78	< 0.0001	2.16	1.89	2.48	< 0.0001	3.35	2.87	3.91	< 0.0001	0.68
Model 3	2574	229644	1.26	1.13	1.40	< 0.0001	1.53	1.36	1.72	< 0.0001	2.00	1.74	2.30	< 0.0001	2.85	2.42	3.36	< 0.0001	0.70
Atrial fibrillation																			
Model 1	8201	237201	1.38	1.30	1.47	< 0.0001	1.82	1.71	1.94	< 0.0001	2.33	2.16	2.51	< 0.0001	3.15	2.87	3.46	< 0.0001	0.59
Model 2	7960	231808	1.18	1.11	1.25	< 0.0001	1.40	1.31	1.49	< 0.0001	1.69	1.56	1.83	< 0.0001	2.19	1.98	2.41	< 0.0001	0.74
Model 3	7786	228576	1.12	1.06	1.19	0.0001	1.26	1.18	1.35	< 0.0001	1.39	1.28	1.51	< 0.0001	1.60	1.44	1.78	< 0.0001	0.75
CHD																			
Model 1	5998	233058	1.44	1.35	1.55	< 0.0001	1.98	1.84	2.13	< 0.0001	2.65	2.43	2.90	< 0.0001	4.26	3.84	4.73	< 0.0001	0.61
Model 2	5816	227844	1.27	1.18	1.36	< 0.0001	1.59	1.47	1.71	< 0.0001	1.96	1.79	2.15	< 0.0001	2.92	2.62	3.25	< 0.0001	0.69
Model 3	5671	224763	1.21	1.13	1.30	< 0.0001	1.44	1.33	1.56	< 0.0001	1.66	1.51	1.83	< 0.0001	2.23	1.98	2.50	< 0.0001	0.70
Heart failure																			
Model 1	4400	238819	1.53	1.40	1.67	< 0.0001	2.54	2.32	2.77	< 0.0001	3.73	3.37	4.13	< 0.0001	5.96	5.32	6.67	< 0.0001	0.65
Model 2	4235	233400	1.26	1.16	1.38	< 0.0001	1.88	1.71	2.06	< 0.0001	2.56	2.30	2.84	< 0.0001	3.63	3.22	4.10	< 0.0001	0.75
Model 3	4114	230125	1.17	1.07	1.28	0.0007	1.58	1.44	1.74	< 0.0001	1.93	1.73	2.15	< 0.0001	2.38	2.09	2.70	< 0.0001	0.77

CHD, Cardiovascular heart disease. Model 1 was unadjusted. Model 2 was adjusted as for age, deprivation index, ethnicity, alcohol intake and dietary intakes. Model 3 (fully adjusted) was adjusted as in model 2 but also included lifestyle factors (smoking status, physical activity, time spent using TV/CPU), and BMI. The incremental effect of increasing number of IC factors was assessed by comparing the HRs for the presence of one, two, three, or four indicators, using the cero factors as the reference group. The number of missing data in model 1 to 3 are derived for the variables as: education, income, race, Townsend index, smoking status, alcohol consumption, BMI and sedentary behavior. * The values for the number of affected were based on complete cases.

Table S5. Association of incidence of all-causes cardiovascular disease by intrinsic capacity factors for sex and age group (n = 384 380): univariate and multivariate analysis model.

Morbidity age-sex groups	Affected *	1 factor (better IC)					2 factors				3 factors				+4 factors (deficit IC)				C-index
		Total	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	
Males (37-56 years)																			
Model 1	8114	62484	1.31	1.24	1.38	< 0.0001	1.62	1.52	1.72	< 0.0001	1.92	1.75	2.10	< 0.0001	2.78	2.41	3.19	< 0.0001	0.56
Model 2	7814	60666	1.27	1.20	1.34	< 0.0001	1.52	1.43	1.62	< 0.0001	1.78	1.62	1.95	< 0.0001	2.39	2.06	2.77	< 0.0001	0.61
Model 3	7743	60244	1.20	1.14	1.26	< 0.0001	1.35	1.27	1.44	< 0.0001	1.45	1.32	1.60	< 0.0001	1.79	1.53	2.09	< 0.0001	0.65
Males (56-65 years)																			
Model 1	12330	48201	1.12	1.07	1.17	< 0.0001	1.30	1.24	1.37	< 0.0001	1.53	1.42	1.64	< 0.0001	1.98	1.77	2.21	< 0.0001	0.54
Model 2	11975	46955	1.11	1.06	1.16	< 0.0001	1.27	1.21	1.34	< 0.0001	1.44	1.34	1.55	< 0.0001	1.83	1.63	2.05	< 0.0001	0.57
Model 3	11872	46602	1.07	1.03	1.12	0.0021	1.17	1.11	1.24	< 0.0001	1.25	1.16	1.35	< 0.0001	1.46	1.29	1.65	< 0.0001	0.60
Males (+65 years)																			
Model 1	9466	25697	1.12	1.06	1.18	< 0.0001	1.21	1.14	1.28	< 0.0001	1.41	1.30	1.53	< 0.0001	1.81	1.60	2.06	< 0.0001	0.53
Model 2	9116	24865	1.11	1.05	1.17	0.0001	1.17	1.10	1.24	< 0.0001	1.36	1.26	1.48	< 0.0001	1.72	1.51	1.96	< 0.0001	0.55
Model 3	8974	24539	1.08	1.03	1.14	0.0037	1.11	1.04	1.17	0.0010	1.23	1.13	1.34	< 0.0001	1.49	1.30	1.70	< 0.0001	0.58
Males (Full sample)																			
Model 1	29910	136382	1.25	1.22	1.29	< 0.0001	1.48	1.43	1.53	< 0.0001	1.77	1.69	1.86	< 0.0001	2.41	2.24	2.59	< 0.0001	0.55
Model 2	28905	132486	1.15	1.12	1.19	< 0.0001	1.30	1.26	1.34	< 0.0001	1.50	1.43	1.58	< 0.0001	1.94	1.80	2.09	< 0.0001	0.66
Model 3	28589	131385	1.11	1.08	1.14	< 0.0001	1.20	1.16	1.24	< 0.0001	1.29	1.23	1.36	< 0.0001	1.56	1.45	1.69	< 0.0001	0.68
Females (37-56 years)																			
Model 1	7216	83668	1.44	1.36	1.53	< 0.0001	1.88	1.76	2.01	< 0.0001	2.76	2.54	3.01	< 0.0001	4.45	3.99	4.95	< 0.0001	0.60
Model 2	6999	82095	1.35	1.27	1.43	< 0.0001	1.65	1.54	1.77	< 0.0001	2.31	2.12	2.52	< 0.0001	3.43	3.06	3.84	< 0.0001	0.63
Model 3	6899	81354	1.24	1.16	1.31	< 0.0001	1.37	1.28	1.47	< 0.0001	1.69	1.54	1.85	< 0.0001	2.34	2.08	2.64	< 0.0001	0.68
Females (56-65 years)																			
Model 1	12095	68255	1.28	1.22	1.34	< 0.0001	1.59	1.51	1.67	< 0.0001	2.00	1.87	2.14	< 0.0001	2.62	2.39	2.87	< 0.0001	0.57
Model 2	11763	66749	1.25	1.19	1.31	< 0.0001	1.51	1.43	1.59	< 0.0001	1.83	1.71	1.96	< 0.0001	2.27	2.06	2.49	< 0.0001	0.60
Model 3	11541	65895	1.18	1.13	1.24	< 0.0001	1.36	1.29	1.43	< 0.0001	1.53	1.43	1.64	< 0.0001	1.69	1.53	1.87	< 0.0001	0.63
Females (+65 years)																			
Model 1	9529	32317	1.13	1.07	1.19	< 0.0001	1.32	1.25	1.40	< 0.0001	1.66	1.54	1.79	< 0.0001	2.04	1.83	2.26	< 0.0001	0.55
Model 2	9286	31515	1.11	1.05	1.17	0.0001	1.27	1.19	1.34	< 0.0001	1.55	1.44	1.67	< 0.0001	1.86	1.67	2.07	< 0.0001	0.57
Model 3	9076	30942	1.08	1.02	1.14	0.0060	1.18	1.11	1.25	< 0.0001	1.38	1.27	1.49	< 0.0001	1.53	1.37	1.71	< 0.0001	0.60
Females (Full sample)																			
Model 1	28840	184240	1.39	1.35	1.43	< 0.0001	1.79	1.73	1.85	< 0.0001	2.35	2.26	2.45	< 0.0001	3.18	3.00	3.37	< 0.0001	0.58
Model 2	28048	180359	1.23	1.20	1.27	< 0.0001	1.47	1.42	1.52	< 0.0001	1.84	1.77	1.93	< 0.0001	2.37	2.24	2.52	< 0.0001	0.68
Model 3	27516	178191	1.17	1.13	1.20	< 0.0001	1.30	1.26	1.35	< 0.0001	1.52	1.45	1.59	< 0.0001	1.78	1.67	1.89	< 0.0001	0.70

Model 1 was unadjusted. Model 2 was adjusted as for age, deprivation index, ethnicity, alcohol intake and dietary intakes. Model 3 (fully adjusted) was adjusted as in model 2 but also included lifestyle factors (smoking status, physical activity, time spent using TV/CPU), and BMI. The incremental effect of increasing number of IC factors was assessed by comparing the HRs for the presence of one, two, three, or four indicators, using the cero factors as the reference group. The number of missing data in

model 1 to 3 are derived for the variables as: education, income, race, Townsend index, smoking status, alcohol consumption, BMI and sedentary behavior. * The values for the number of affected were based on complete cases.

Table S6. Association of mortality of all-causes cardiovascular disease by intrinsic capacity factors for sex and age group (n= 443 130) univariate and multivariate analysis model.

Mortality age-sex groups	Affected *	1 factor (better IC)				2 factors				3 factors				+4 factors (deficit IC)				C-index
		Total	HR	IC95%	p-value	HR	IC95%		p-value	HR	IC95%		p-value	HR	IC95%		p-value	
Males (37-56 years)																		
Model 1	466	76853	1.31	1.02	1.68	0.0314	1.97	1.51	2.58	< 0.0001	3.97	2.93	5.39	< 0.0001	8.66	6.11	12.28	< 0.0001	0.63
Model 2	437	74558	1.19	0.93	1.53	0.1668	1.59	1.21	2.10	0.0010	3.04	2.21	4.19	< 0.0001	4.69	3.16	6.96	< 0.0001	0.70
Model 3	434	73999	1.11	0.86	1.43	0.4147	1.33	1.01	1.77	0.0442	2.30	1.65	3.19	< 0.0001	2.85	1.87	4.33	< 0.0001	0.74
Males (56-65 years)																		
Model 1	1380	75976	1.27	1.10	1.47	0.0015	1.76	1.50	2.06	< 0.0001	2.74	2.28	3.30	< 0.0001	4.34	3.52	5.35	< 0.0001	0.60
Model 2	1315	73811	1.19	1.03	1.39	0.0209	1.58	1.34	1.86	< 0.0001	2.16	1.78	2.62	< 0.0001	3.09	2.47	3.86	< 0.0001	0.65
Model 3	1294	73152	1.14	0.98	1.33	0.0820	1.38	1.17	1.63	0.0001	1.71	1.40	2.09	< 0.0001	2.02	1.59	2.56	< 0.0001	0.70
Males (+65 years)																		
Model 1	1826	50193	1.05	0.92	1.19	0.4640	1.43	1.25	1.64	< 0.0001	1.81	1.54	2.13	< 0.0001	3.06	2.54	3.68	< 0.0001	0.58
Model 2	1734	48460	1.03	0.90	1.18	0.6639	1.34	1.17	1.54	< 0.0001	1.61	1.36	1.90	< 0.0001	2.69	2.21	3.26	< 0.0001	0.62
Model 3	1699	47764	0.99	0.87	1.13	0.9002	1.21	1.05	1.40	0.0075	1.32	1.11	1.58	0.0015	1.97	1.60	2.42	< 0.0001	0.66
Males (Full sample)																		
Model 1	3672	203022	1.29	1.18	1.41	< 0.0001	1.89	1.72	2.08	< 0.0001	2.84	2.54	3.18	< 0.0001	4.99	4.39	5.68	< 0.0001	0.61
Model 2	3486	196829	1.12	1.02	1.23	0.0179	1.48	1.34	1.63	< 0.0001	1.94	1.72	2.18	< 0.0001	3.04	2.65	3.49	< 0.0001	0.73
Model 3	3427	194915	1.07	0.97	1.17	0.1705	1.31	1.18	1.44	< 0.0001	1.56	1.38	1.76	< 0.0001	2.10	1.81	2.43	< 0.0001	0.75
Females (37-56 years)																		
Model 1	196	95926	1.51	1.02	2.24	0.0377	2.46	1.63	3.73	< 0.0001	4.27	2.66	6.85	< 0.0001	7.09	4.15	12.13	< 0.0001	0.65
Model 2	185	94047	1.42	0.94	2.13	0.0929	2.01	1.30	3.10	0.0016	2.93	1.77	4.86	< 0.0001	4.02	2.25	7.18	< 0.0001	0.73
Model 3	180	93119	1.28	0.85	1.93	0.2313	1.56	1.00	2.44	0.0508	2.03	1.19	3.45	0.0091	2.30	1.22	4.35	0.0102	0.76
Females (56-65 years)																		
Model 1	540	92164	1.13	0.89	1.45	0.3193	1.74	1.36	2.24	< 0.0001	2.62	1.97	3.48	< 0.0001	4.77	3.52	6.45	< 0.0001	0.62
Model 2	515	89994	1.10	0.85	1.42	0.4582	1.64	1.27	2.12	0.0002	2.27	1.69	3.06	< 0.0001	3.65	2.64	5.06	< 0.0001	0.67
Model 3	491	88688	1.05	0.81	1.35	0.7138	1.45	1.11	1.88	0.0058	1.81	1.32	2.47	0.0002	2.50	1.75	3.57	< 0.0001	0.70
Females (+65 years)																		
Model 1	857	51504	1.29	1.06	1.57	0.0115	1.63	1.33	2.00	< 0.0001	2.03	1.60	2.58	< 0.0001	3.53	2.73	4.57	< 0.0001	0.59
Model 2	824	50106	1.24	1.02	1.52	0.0314	1.47	1.19	1.81	0.0003	1.73	1.35	2.22	< 0.0001	2.96	2.26	3.87	< 0.0001	0.64
Model 3	792	49052	1.21	0.99	1.48	0.0692	1.33	1.07	1.65	0.0096	1.43	1.10	1.86	0.0067	2.14	1.60	2.85	< 0.0001	0.68
Females (Full sample)																		
Model 1	1593	239594	1.46	1.27	1.69	< 0.0001	2.19	1.89	2.54	< 0.0001	3.12	2.63	3.71	< 0.0001	5.56	4.63	6.69	< 0.0001	0.63
Model 2	1524	234147	1.23	1.07	1.43	0.0049	1.62	1.39	1.88	< 0.0001	2.06	1.72	2.46	< 0.0001	3.36	2.76	4.08	< 0.0001	0.77
Model 3	1463	230859	1.18	1.01	1.36	0.0318	1.42	1.22	1.66	< 0.0001	1.65	1.37	1.98	< 0.0001	2.29	1.85	2.84	< 0.0001	0.78

Model 1 was unadjusted. Model 2 was adjusted as for age, deprivation index, ethnicity, alcohol intake and dietary intakes. Model 3 (fully adjusted) was adjusted as in model 2 but also included lifestyle factors (smoking status, physical activity, time spent using TV/CPU), and BMI. The incremental effect of increasing number of IC factors

was assessed by comparing the HRs for the presence of one, two, three, or four indicators, using the cero factors as the reference group. The number of missing data in model 1 to 3 are derived for the variables as: education, income, race, Townsend index, smoking status, alcohol consumption, BMI and sedentary behavior. * The values for the number of affected were based on complete cases.

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