

Multimorbidity Patterns and Risk of Frailty in Older Community-Dwelling Adults: A Population-Based Cohort Study

Supplemental Material

Supplementary Figure S1: Study population derived from SNAC-K

Supplementary Table S1: Baseline characteristics by missing physical frailty status (n=2741)

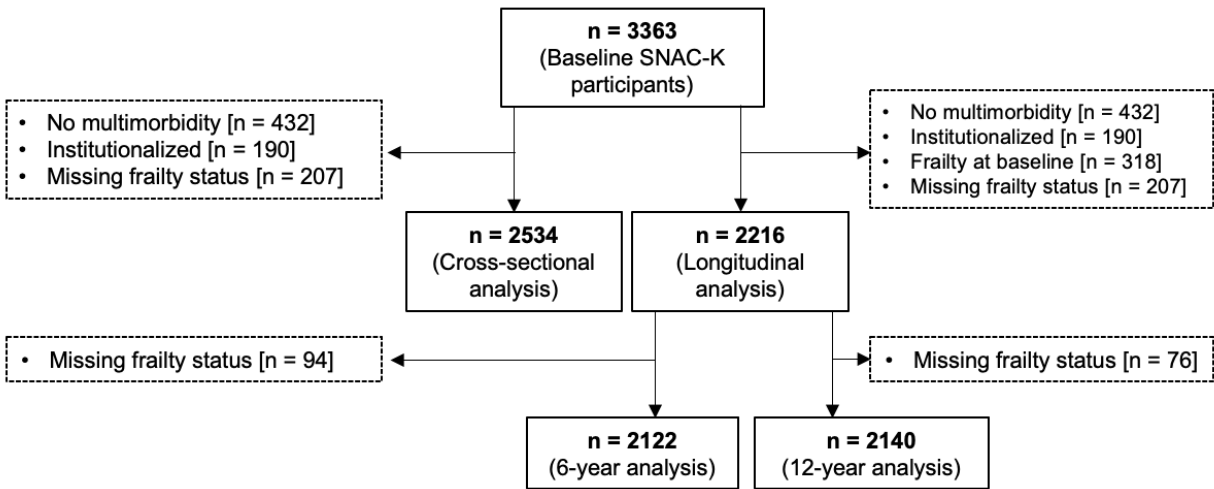
Supplementary Table S2: Prevalence, observed/expected ratio, and exclusivity of diseases within multimorbidity patterns

Supplementary Table S3: Prevalence of chronic diseases in study population at baseline (n=2534)

Supplementary Table S4: Six- (n=2122) and 12- (n=2140) year associations between multimorbidity patterns and physical frailty, death, and dropping out in complete cases

Supplementary Table S5: Cross-sectional (n=2741) and longitudinal associations (n=2423) between multimorbidity patterns and physical frailty in imputed population at six and 12 years

Supplementary Table S6: Cross-sectional (n=2534) and six (n=2122) and 12 (n=2140) year longitudinal associations of multimorbidity patterns with frailty in complete cases by sex and age



Supplementary Figure S1: Study population derived from SNAC-K

Supplementary Table S1: Baseline characteristics by missing physical frailty status (n=2741)

Characteristics	Not missing frailty (n = 2534)	Missing frailty (n = 207)	p-value
Age (years)	74.3 ± 10.3	85.9 ± 8.5	< 0.001
Sex (female)	1631 (64.4)	158 (76.3)	0.001
Education			
Elementary	437 (17.3)	54 (27.4)	< 0.001
High school	1270 (50.2)	120 (60.9)	0.004
University	825 (32.6)	23 (11.7)	< 0.001
Civil status			
Partnered	1158 (45.7)	49 (24.5)	< 0.001
Widowed	664 (26.2)	101 (50.5)	< 0.001
Unmarried	371 (14.7)	27 (13.5)	0.656
Divorced	339 (13.4)	23 (11.5)	0.448
Alcohol consumption			
Never/occasional	913 (36.3)	125 (66.8)	< 0.001
Light/moderate	1186 (47.1)	49 (26.2)	< 0.001
Heavy	419 (16.6)	13 (7.0)	< 0.001
Smoking status			
Never	1187 (47.1)	109 (57.4)	0.006
Former	968 (38.4)	61 (32.1)	0.083
Current	364 (14.5)	20 (10.5)	0.135
Number of diseases	4.3 ± 2.1	6.2 ± 2.7	< 0.001
Mortality			
Deceased within six years	528 (20.8)	125 (60.4)	< 0.001
Deceased within 12 years	715 (28.2)	153 (73.9)	< 0.001
Diseases			
Anemia	301 (11.9)	58 (28.0)	< 0.001
Atrial Fibrillation	247 (9.8)	41 (19.8)	< 0.001
Cerebrovascular disease	179 (7.1)	37 (17.9)	< 0.001
Chronic Kidney Disease	942 (37.2)	117 (56.5)	< 0.001
COPD	129 (5.1)	22 (10.6)	0.001
Dementia	105 (4.1)	61 (29.5)	< 0.001
Depression	243 (9.6)	33 (15.9)	0.003
Diabetes	249 (9.8)	27 (13.0)	0.139
Heart Failure	242 (9.6)	59 (28.5)	< 0.001
Hypertension	1936 (76.4)	140 (67.6)	0.005
Ischemic Heart Disease	406 (16.0)	57 (27.5)	< 0.001
Solid Neoplasms	252 (9.9)	28 (13.5)	0.102

Notes: COPD = chronic obstructive pulmonary disease. Values are presented as absolute number and column percentage (%) or mean ± standard deviation.

Supplementary Table S2: Prevalence, observed/expected ratio, and exclusivity of diseases within multimorbidity patterns

Multimorbidity pattern	Disease	Prevalence within pattern (%)	Observed / Expected Ratio	Exclusivity (%)
Psychiatric	Neurotic, stress-related and somatoform diseases	54.45	15.55	95
	Depression and mood diseases	82.57	8.20	50
	Other neurological diseases	6.00	2.89	18
	Asthma	17.54	2.45	15
	Sleep disorders	5.48	2.28	14
	Colitis and related diseases	26.82	2.23	14
	Migraine and facial pain syndromes	4.95	1.97	12
	Other musculoskeletal and joint diseases	12.50	1.80	11
	COPD, emphysema, chronic bronchitis	9.12	1.65	10
	Esophagus, stomach and duodenum diseases	7.86	1.58	10
Cardio., Anemia, & Dementia	Bradycardias and conduction diseases	18.88	9.08	80
	Other cardiovascular diseases	25.51	6.92	61
	Heart failure	71.59	6.52	57
	Cardiac valve diseases	17.82	6.11	54
	Atrial fibrillation	58.23	5.54	49
	Cerebrovascular disease	26.74	3.39	30
	Ischemic heart disease	51.85	3.07	27
	Anemia	37.25	2.84	25
Sensory & Cancer	Dementia	17.20	2.84	25
	Inflammatory arthropathies	11.71	2.57	23
	Cataract and other lens diseases	35.98	5.87	69
	Blindness, visual impairment	24.40	5.72	67
	Other eye diseases	33.09	5.70	67
	Glaucoma	26.79	4.42	52
	Deafness, hearing impairment	34.82	3.00	35
	Solid neoplasms	21.93	2.15	25
	Other genitourinary diseases	5.67	1.97	23
	Dementia	11.83	1.95	23
Metabolic & Sleep	Anemia	22.77	1.74	20
	Chronic kidney diseases	65.36	1.69	20
	Diabetes	37.96	3.77	42
	Sleep disorders	7.62	3.16	36
	Obesity	38.64	2.79	31
	Ischemic heart disease	33.50	1.98	22
	Inflammatory arthropathies	9.02	1.98	22
	Other cardiovascular diseases	6.34	1.72	19
	Dementia	10.29	1.70	19
	Prostate diseases	7.56	1.63	18

Multimorbidity pattern	Disease	Prevalence within pattern (%)	Observed / Expected Ratio	Exclusivity (%)
Metabolic & Sleep (continued)	COPD, emphysema, chronic bronchitis	8.17	1.48	17
	Heart failure	16.13	1.47	16
MSK, Resp., & GI	Osteoporosis	31.41	4.26	67
	Dorsopathies	21.80	2.93	46
	Esophagus, stomach and duodenum diseases	14.21	2.86	45
	Asthma	19.98	2.79	44
	COPD, emphysema, chronic bronchitis	12.77	2.32	37
	Autoimmune diseases	11.67	2.28	36
	Inflammatory arthropathies	9.07	1.99	31
	Thyroid diseases	22.74	1.96	31
	Colitis and related diseases	22.95	1.91	30
	Osteoarthritis and other degenerative joint diseases	27.58	1.88	30
	Unspecific	Dyslipidemia	67.35	1.28
Hypertension		84.61	1.12	52
Obesity		13.07	0.94	44
Prostate diseases		4.29	0.93	43
Other musculoskeletal and joint diseases		5.83	0.84	39
Other genitourinary diseases		2.42	0.84	39
Solid neoplasms		7.86	0.77	36
Migraine and facial pain syndromes		1.88	0.75	35
Thyroid diseases		8.56	0.74	34
Osteoarthritis and other degenerative joint diseases		10.63	0.72	34

Notes: COPD = chronic obstructive pulmonary disease; Cardio., Anemia, & Dementia = Cardiovascular Diseases, Anemia, & Dementia; Sensory & Cancer = Sensory Impairments & Cancer; Metabolic & Sleep = Metabolic & Sleep Disorders; MSK, Resp., & GI = Musculoskeletal, Respiratory, & Gastrointestinal Diseases. Shaded cells refer to Observed/Expected ratios > 2 and Exclusivity ≥ 25.

Supplementary Table S3: Prevalence of chronic diseases in study population at baseline (n=2534)

Disease	Number	Prevalence (%)
Hypertension	1936	76
Dyslipidemia	1369	54
Chronic kidney diseases	942	37
Ischemic heart disease	406	16
Osteoarthritis and other degenerative joint diseases	374	15
Obesity	369	15
Anemia	301	12
Thyroid diseases	291	11
Colitis and related diseases	278	11
Deafness, hearing impairment	262	10
Solid neoplasms	252	10
Diabetes	249	10
Atrial Fibrillation	247	10
Depression and mood diseases	243	10
Heart failure	242	10
Dorsopathies	191	8
Cerebrovascular disease	179	7
Asthma	178	7
Osteoporosis	176	7
Other musculoskeletal and joint diseases	164	6
Cataract and other lens diseases	146	6
Glaucoma	142	6
Other eye diseases	140	6
COPD, emphysema, chronic bronchitis	129	5
Esophagus, stomach and duodenum diseases	126	5
Autoimmune diseases	125	5
Prostate diseases	119	5
Inflammatory Arthropathies	112	4
Dementia	105	4
Other cardiovascular diseases	89	4
Blindness, visual impairment	85	3
Neurotic, stress-related and somatoform diseases	85	3
Other genitourinary diseases	74	3
Cardiac valve diseases	70	3
Sleep disorders	61	2
Migraine and facial pain syndromes	60	2
Other neurological diseases	51	2
Bradycardias and conduction diseases	47	2

Notes: COPD = chronic obstructive pulmonary disease

Supplementary Table S4: Six- (n=2122) and 12- (n=2140) year associations between multimorbidity patterns and physical frailty, death, and dropping out in complete cases

Pattern	Six-year		12-year	
	RRR	95% CI	RRR	95% CI
Frail				
Unspecific	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	1.22	0.78-1.92	1.38	0.94-2.03
Metabolic & Sleep	1.99	1.25-3.16	1.43	0.93-2.19
Sensory & Cancer	1.36	0.82-2.25	1.87	1.05-3.35
Cardio., Anemia, & Dementia	2.25	1.13-4.49	4.81	1.59-14.60
Psychiatric	3.04	1.59-5.79	2.62	1.45-4.72
Deceased				
Unspecific	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	1.19	0.78-1.83	1.05	0.70-1.57
Metabolic & Sleep	2.03	1.33-3.09	1.49	0.98-2.27
Sensory & Cancer	1.46	0.92-2.31	1.58	0.89-2.81
Cardio., Anemia, & Dementia	4.79	2.68-8.57	7.98	2.71-23.49
Psychiatric	2.00	1.03-3.90	2.29	1.24-4.23
Dropped out				
Unspecific	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	0.99	0.68-1.45	1.13	0.79-1.61
Metabolic & Sleep	1.36	0.91-2.02	1.14	0.77-1.71
Sensory & Cancer	0.90	0.54-1.50	1.21	0.66-2.19
Cardio., Anemia, & Dementia	1.64	0.82-3.30	3.52	1.15-10.81
Psychiatric	1.57	0.90-2.73	1.86	1.08-3.21

Notes: MSK, Resp., & GI = Musculoskeletal, Respiratory, & Gastrointestinal Diseases; Metabolic & Sleep = Metabolic & Sleep Disorders; Sensory & Cancer = Sensory Impairments & Cancer; Cardio., Anemia, & Dementia = Cardiovascular Diseases, Anemia, & Dementia; RRR = relative risk ratio. Missing six-year analysis observations: education (n=1), civil status (n=2), alcohol consumption (n=8), smoking status (n=11). Missing 12-year analysis observations: education (n=1), civil status (n=1), alcohol consumption (n=9), smoking status (n=10). Model adjusted for age, sex, education, civil status, smoking status, and alcohol consumption. Reference outcome is non-frail participants who did not die or drop out at six or 12 years.

Supplementary Table S5: Cross-sectional (n=2741) and longitudinal associations (n=2423) between multimorbidity patterns and physical frailty in imputed population at six and 12 years

Pattern	Cases		Model 1		Model 2	
Cross-sectional	n/N	%	OR	95% CI	OR	95% CI
Unspecific	63 / 1245	5.1	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	80 / 435	18.3	3.13	2.13-4.62	3.07	2.07-4.54
Metabolic & Sleep	28 / 306	9.0	1.77	1.05-2.97	1.67	0.99-2.82
Sensory & Cancer	95 / 344	27.6	2.62	1.75-3.90	2.44	1.62-3.67
Cardio., Anemia, & Dementia	107 / 245	43.5	5.58	3.66-8.51	5.31	3.46-8.13
Psychiatric	35 / 166	21.0	5.21	2.94-9.26	5.10	2.85-9.10
Six-year	n/N	%	RRR	95% CI	RRR	95% CI
Unspecific	102 / 1189	8.6	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	50 / 369	13.7	1.35	0.89-2.05	1.34	0.88-2.04
Metabolic & Sleep	38 / 281	13.7	1.94	1.22-3.07	1.94	1.22-3.08
Sensory & Cancer	59 / 275	21.3	1.33	0.85-2.06	1.30	0.83-2.02
Cardio., Anemia, & Dementia	31 / 169	18.5	2.44	1.21-4.94	2.35	1.14-4.82
Psychiatric	24 / 140	17.3	3.36	1.88-6.01	3.27	1.81-5.90
12-year	n/N	%	RRR	95% CI	RRR	95% CI
Unspecific	204 / 1189	17.2	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	88 / 369	24.0	1.49	1.00-2.22	1.44	0.96-2.15
Metabolic & Sleep	62 / 281	21.9	1.55	0.98-2.44	1.51	0.96-2.38
Sensory & Cancer	83 / 275	30.3	2.18	1.18-4.03	2.07	1.10-3.88
Cardio., Anemia, & Dementia	37 / 169	22.0	6.18	2.06-18.52	5.64	1.89-16.82
Psychiatric	31 / 140	22.4	2.55	1.43-4.54	2.37	1.32-4.24

Notes: MSK, Resp., & GI = Musculoskeletal, Respiratory, & Gastrointestinal Diseases; Metabolic & Sleep = Metabolic & Sleep Disorders; Sensory & Cancer = Sensory Impairments & Cancer; Cardio., Anemia, & Dementia = Cardiovascular Diseases, Anemia, & Dementia; OR = odds ratio, RRR = relative risk ratio. Figures reported are based on five imputed datasets. Imputed observations in cross-sectional model: civil status (n=9), education (n=12), smoking status (n=32), alcohol consumption (n=36), baseline frailty status (n=207). Imputed observations in longitudinal model: civil status (n=9), education (n=11), smoking status (n=28), alcohol consumption (n=29), six-year frailty status (n=301), 12-year frailty status (n=283). Model 1: adjusted for age, sex, and education. Model 2: adjusted for age, sex, education, civil status, smoking status, and alcohol consumption.

Supplementary Table S6: Cross-sectional (n=2534) and six (n=2122) and 12 (n=2140) year longitudinal associations of multimorbidity patterns with frailty in complete cases by sex and age

Pattern	Cross-sectional		Six-year		12-year	
	OR	95% CI	RRR	95% CI	RRR	95% CI
Female						
Unspecific	1 (ref)	-	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	2.97	1.82-4.82	1.21	0.71-2.04	1.39	0.88-2.19
Metabolic & Sleep	1.64	0.80-3.35	1.82	0.94-3.53	1.44	0.77-2.70
Sensory & Cancer	2.53	1.50-4.25	1.37	0.73-2.59	1.86	0.91-3.77
Cardio., Anemia, & Dementia	6.57	3.85-11.21	3.34	1.42-7.84	7.36	1.58-34.38
Psychiatric	5.35	2.74-10.45	2.90	1.33-6.31	2.96	1.51-5.82
Male						
Unspecific	1 (ref)	-	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	4.77	2.19-10.37	1.13	0.43-2.93	0.50	0.24-1.04
Metabolic & Sleep	1.95	0.90-4.24	2.05	1.06-3.98	0.61	0.34-1.09
Sensory & Cancer	2.10	0.96-4.57	1.34	0.58-3.09	0.43	0.15-1.19
Cardio., Anemia, & Dementia	3.92	1.74-8.83	0.83	0.21-3.31	0.10	0.02-0.47
Psychiatric	4.29	1.57-11.70	3.67	1.10-12.23	0.33	0.09-1.17
< 78 years						
Unspecific	1 (ref)	-	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	6.36	2.62-15.44	1.69	0.72-3.96	1.56	0.93-2.60
Metabolic & Sleep	4.09	1.59-10.51	2.60	1.21-5.59	1.68	0.99-2.85
Sensory & Cancer	5.11	1.42-18.42	1.96	0.52-7.44	1.59	0.64-3.97
Cardio., Anemia, & Dementia	16.13	5.04-51.67	4.02	0.81-19.94	6.70	1.66-27.00
Psychiatric	7.35	2.58-20.94	3.67	1.44-9.38	2.92	1.47-5.80
≥ 78 years						
Unspecific	1 (ref)	-	1 (ref)	-	1 (ref)	-
MSK, Resp., & GI	2.51	1.58-4.00	0.99	0.56-1.72	0.72	0.36-1.43
Metabolic & Sleep	1.23	0.64-2.36	1.77	0.93-3.36	0.99	0.40-2.47
Sensory & Cancer	2.00	1.27-3.15	1.19	0.68-2.08	2.19	0.78-6.12
Cardio., Anemia, & Dementia	4.09	2.57-6.52	2.14	0.98-4.68	4.38	0.55-34.69
Psychiatric	4.75	2.38-9.46	2.88	1.03-8.09	0.97	0.27-3.43

Notes: MSK, Resp., & GI = Musculoskeletal, Respiratory, & Gastrointestinal Diseases; Metabolic & Sleep = Metabolic & Sleep Disorders; Sensory & Cancer = Sensory Impairments & Cancer; Cardio., Anemia, & Dementia = Cardiovascular Diseases, Anemia, & Dementia; OR = odds ratio, RRR = relative risk ratio. Model adjusted for age, sex, education, civil status, smoking status, and alcohol consumption. Missing cross-sectional observations: civil status (n=2), education (n=2), smoking status (n=15), alcohol consumption (n=16). Missing six-year observations: education (n=1), civil status (n=2), alcohol consumption (n=8), smoking status (n=11). Missing 12-year observations: education (n=1), civil status (n=1), alcohol consumption (n=9), smoking status (n=10).