Multimorbidity, mortality, and long-term physical functioning in three prospective cohorts of community-dwelling adults

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Web Appendix 1. Calculation of the multimorbidity-weighted index.

1. Assess for the presence of physician-diagnosed chronic diseases and conditions using a "yes" or "no" response.

2. Look up the MWI weightings for each chronic disease or condition using Supplemental Table 1 below. For chronic diseases and conditions not specifically listed, use the weighting "other diagnosis" in the first row.

3. Add up all the weighted chronic diseases and conditions to create the multimorbidity-weighted index.

Example:

1. Participant A has chronic conditions X_1, X_2 and X_3.

2. Using Supplemental Table 1, the MWI disease weightings for X_1, X_2 and X_3 are β_{X1}, β_{X2}, and β_{X3}, respectively.

3. Person A has a multimorbidity-weighted index = $\beta_{X1} + \beta_{X2} + \beta_{X3}$.

Full reference on the development and validation of the multimorbidity-weighted index:

Wei MY, Kawachi I, Okereke OI, Mukamal KJ. Diverse cumulative impact of chronic diseases on physical health-related quality of life: implications for a measure of multimorbidity. *American Journal of Epidemiology.* 2016;184(5):357-365.
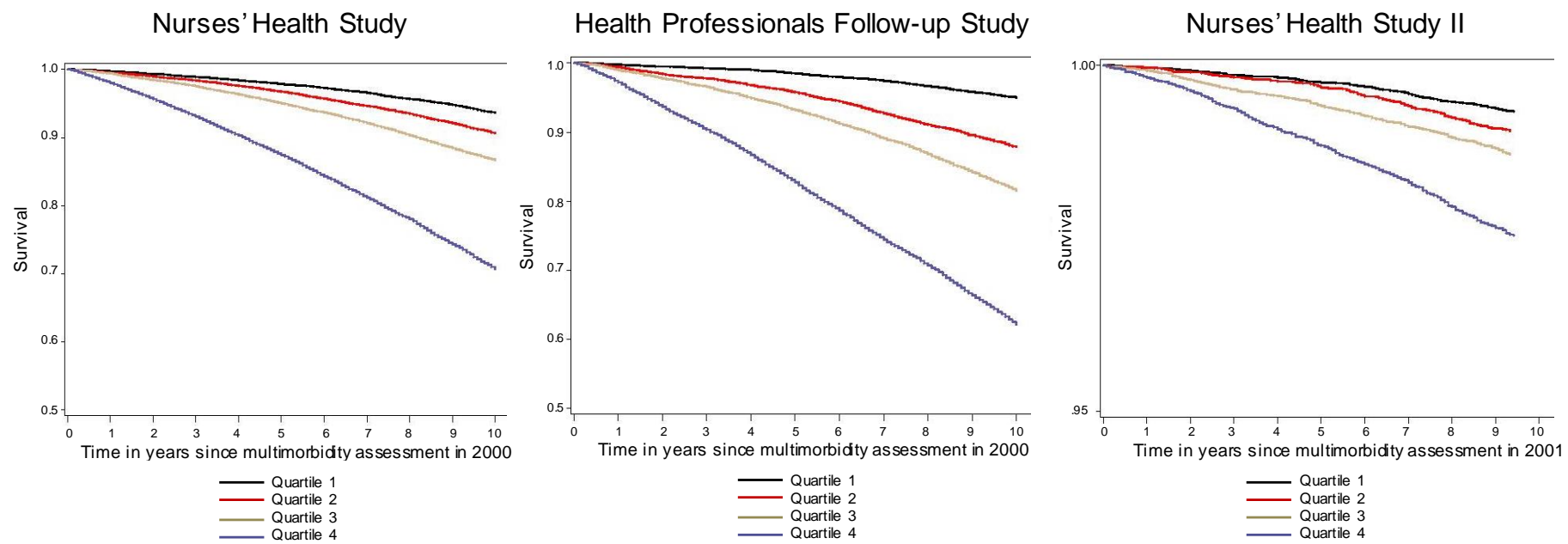
Web Table 1. Multimorbidity-weighted index weightings for self-reported physician-diagnosed chronic diseases and conditions

Chronic disease or condition	Multimorbidity-weighted index weighting
Other diagnosis	-1.46
Cardiovascular	
Angina	-2.20
Aortic aneurysm	-1.96
Atrial fibrillation	-1.33
Automated Implantable Cardioverter Defibrillator (AICD)	-1.57
Congestive heart failure	-4.77
Coronary artery bypass graft surgery	-0.724
High blood pressure	-1.53
Mitral valve prolapse	-0.033
Myocardial infarction	-1.73
Peripheral artery disease	-3.25
Valvular heart disease	-0.416
Aortic insufficiency	
Aortic valve disease	
Aortic valve replacement	
Aortic valve stenosis	
Aortic and mitral valve disorder	
Mitral regurgitation	
Mitral stenosis	
Mitral valve disease	
Mitral valve replacement	
Pulmonary valve disease	
Tricuspid valve disease	
Valve implant	
Endocrine	
Diabetes mellitus	-2.67
Elevated cholesterol	-0.343
Hypercholesterolemia	
Hyperlipidemia	
Hyperthyroidism	-0.149
Grave's disease	
Hypertriglyceridemia	-0.692
Hypothyroidism	-0.808
Thyroid nodule	0
Gastrointestinal	
Barrett's esophagus	-0.284
Chronic hepatitis	-0.293
Hepatocellular disease	
Cirrhosis	-4.30
Liver transplant	
Colon polyp	-0.010
Diverticulosis	-0.624
Diverticulitis	
Gallstones	-0.929
Hepatitis not specified as chronic	-0.147
Inflammatory bowel disease	-1.07
Crohn's disease	
Ulcerative colitis	
Pancreatitis	-0.675
Ulcer, peptic	-1.08
Hematologic	
Pernicious anemia	-1.82
Venous thromboembolism	-1.98
Pulmonary embolus	
Deep venous thrombosis	
Immunologic	
Acquired Immune Deficiency Syndrome (AIDS)	-2.91
Integumentary	
Solar actinic keratosis	0
Musculoskeletal	
Connective tissue disease	-3.02
Sjogren's disease	
Dermatomyositis	
Polymyositis	
Systemic lupus erythematosus	
Gout	-1.34
Herniated disc	-3.27
Hip fracture	-3.56
Hip replacement surgery	-3.55
Knee replacement surgery	-9.11
Osteoarthritis	-3.52
Osteoporosis	-0.997
Rheumatoid arthritis	-3.79
Vertebral fracture	-2.07
Wrist fracture	0
Nervous	
Amyotrophic lateral sclerosis (ALS)	-7.45
Dementia	-6.10
Alzheimer disease	
Migraine headache	-0.614
Multiple sclerosis	-10.6
Parkinson disease	-8.82
Restless legs syndrome	-2.23
Seizure disorder	-0.841
Epilepsy	
Stroke	-3.79
Transient ischemic attack	-1.24
Oncologic	
Basal cell carcinoma	0
Bladder cancer	-0.99
Breast cancer	-0.886
Cervical cancer	-0.723
Colon cancer	-1.18
Leukemia	-1.32
Lymphoma	
Lung cancer	-6.25
Melanoma	0
Other cancer	-1.76
Ovarian cancer	-1.87
Prostate cancer	-0.402
Squamous cell carcinoma	0
Uterine cancer	-0.753
Ophthalmologic	
Cataract	-0.288
Glaucoma	-0.427
Macular degeneration	-0.564
Oral	
Periodontal disease	-0.164
Psychiatric	
Alcohol abuse	-1.37
Depression	-1.29
Pulmonary	
Asthma	-1.62
Chronic obstructive pulmonary disease (COPD)	-4.32
Chronic bronchitis	
Emphysema	
Renal	
Chronic kidney disease	-3.98
Glomerulonephritis	
Kidney failure	
Kidney transplant	
Renal artery occlusion	
Renal artery stenosis	
Interstitial cystitis	-0.879
Kidney stones	-0.291
Reproductive	
Benign breast disease	0
Benign prostatic hyperplasia (BPH)	0
Ectopic pregnancy	0
Endometriosis	-0.142
Erectile dysfunction	-1.22
Polycystic ovary syndrome	-0.640
Premenstrual syndrome	-0.412
Prostate surgery for benign prostatic hyperplasia	0
Uterine fibroid	-0.029

Web Figure 1. Kaplan-Meier survival curves by unadjusted Multimorbidity-Weighted Index quartiles.

Web Table 2. Fully adjusted[a] hazard ratios for mortality after 10-year follow-up.

	Nurses' Health Study	Health Professionals Follow-up Study	Nurses' Health Study II	Meta-analyzed combined cohorts
No. of participants	92,352	32,476	95,122	219,950
Deaths	13,728	6,444	1,320	23,709
Model	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Multimorbidity- Weighted Index, quartiles				
Q4 vs Q1	3.10 (2.88, 3.33)	3.02 (2.67, 3.41)	2.61 (2.04, 3.35)	3.05 (2.99, 3.11)
Q3 vs Q1	1.59 (1.47, 1.71)	1.77 (1.56, 2.00)	1.65 (1.526 2.15)	1.63 (1.57, 1.70)
Q2 vs Q1	1.31 (1.21, 1.42)	1.41 (1.24, 1.60)	1.40 (1.105 1.85)	1.34 (1.27, 1.41)
Q1 (reference)	1.0	1.0	1.0	1.0
	P trend <0.001	*P* trend <0.001	*P* trend <0.001	*P* trend <0.001
Simple Disease Count, quartiles				
Q4 vs Q1	2.60 (2.42, 2.79)	2.46 (2.09, 2.89)	2.41 (1.87, 3.10)	2.57 (2.50, 2.63)
Q3 vs Q1	1.51 (1.41 1.63)	1.49 (1.27, 1.76)	1.40 (1.05, 1.86)	1.50 (1.44, 1.57)
Q2 vs Q1	1.22 (1.12, 1.33)	1.15 (0.96, 1.37)	1.42 (1.07, 1.87)	1.22 (1.15, 1.29)
Q1 (reference)	1.0	1.0	1.0	1.0
	P trend <0.001	*P* trend <0.001	*P* trend <0.001	*P* trend <0.001
Charlson Comorbidity Index[b]				
Q4 vs. Q1-3	2.41 (2.31, 2.52)	1.99 (1.88, 2.11)	N/A[c]	2.26 (2.23, 2.30)
Q1-3 (reference)	1.0	1.0		1.0
	P trend <0.001	*P* trend <0.001		*P* trend <0.001

Abbreviations: AIC, Akaike Information Criterion; CI, confidence interval; HR, hazard ratio; N/A, not available – not calculable; Q, quartile
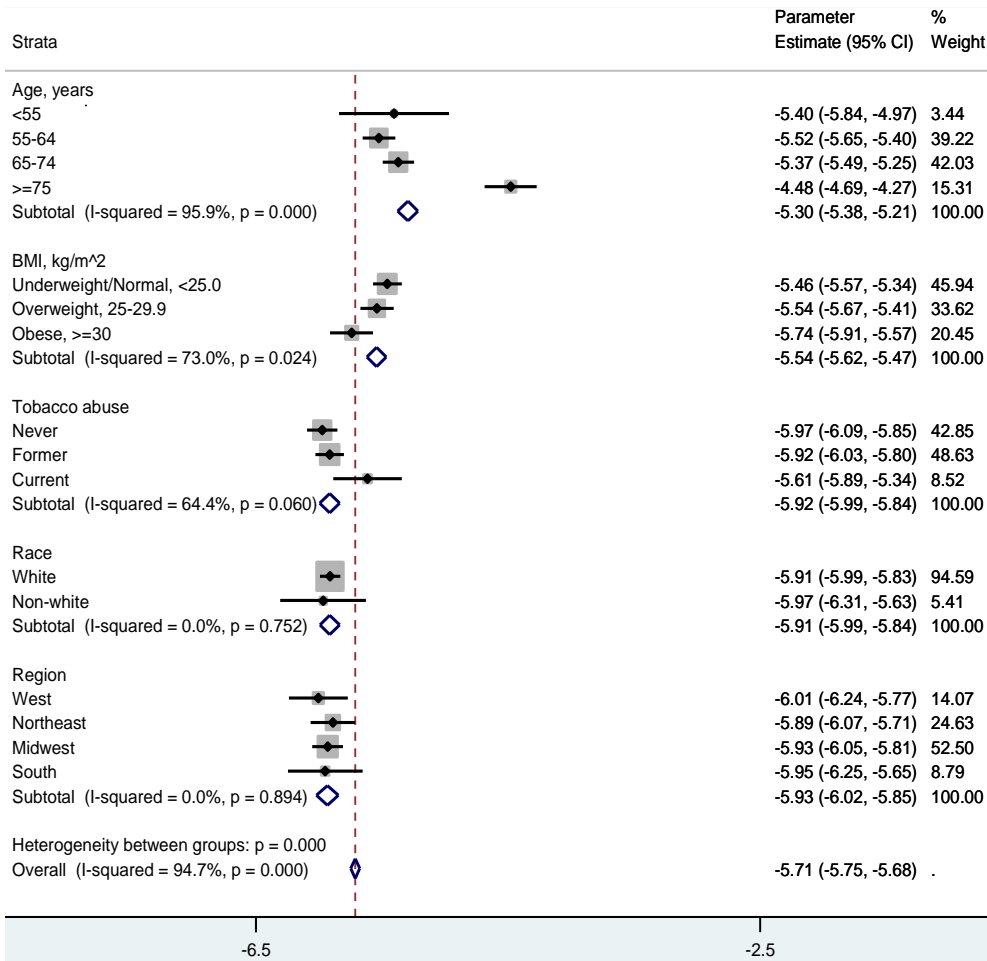
[a] Adjusted for age, race, body mass index, smoking status, alcohol intake, geographic region

[b] Due to a strong left skew, quartiles 1-3 serve as referent group, and the Charlson index cannot be directly compared with the MWI and simple disease count, where quartile 1 serves as the referent group.
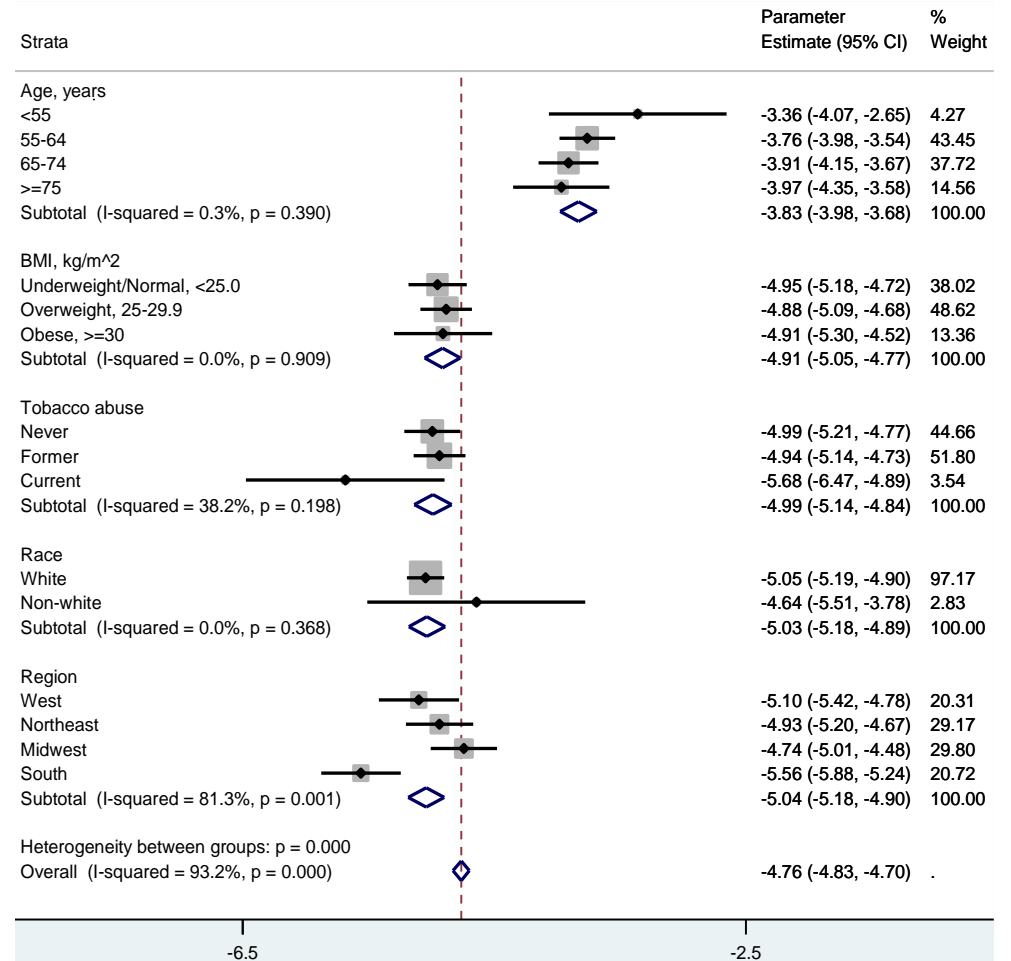
[c] Charlson index not computable in quartiles due to a strong left skew.

Web Figure 2. Future physical functioning by participant characteristics and adjusted overall estimate for each point increase in the standardized Multimorbidity-Weighted Index.

4-year physical functioning in the Nurses' Health Study

Strata	Parameter Estimate (95% CI)	% Weight
Age, years		
<55	-5.40 (-5.84, -4.97)	3.44
55-64	-5.52 (-5.65, -5.40)	39.22
65-74	-5.37 (-5.49, -5.25)	42.03
>=75	-4.48 (-4.69, -4.27)	15.31
Subtotal (I-squared = 95.9%, p = 0.000)	-5.30 (-5.38, -5.21)	100.00
BMI, kg/m^2		
Underweight/Normal, <25.0	-5.46 (-5.57, -5.34)	45.94
Overweight, 25-29.9	-5.54 (-5.67, -5.41)	33.62
Obese, >=30	-5.74 (-5.91, -5.57)	20.45
Subtotal (I-squared = 73.0%, p = 0.024)	-5.54 (-5.62, -5.47)	100.00
Tobacco abuse		
Never	-5.97 (-6.09, -5.85)	42.85
Former	-5.92 (-6.03, -5.80)	48.63
Current	-5.61 (-5.89, -5.34)	8.52
Subtotal (I-squared = 64.4%, p = 0.060)	-5.92 (-5.99, -5.84)	100.00
Race		
White	-5.91 (-5.99, -5.83)	94.59
Non-white	-5.97 (-6.31, -5.63)	5.41
Subtotal (I-squared = 0.0%, p = 0.752)	-5.91 (-5.99, -5.84)	100.00
Region		
West	-6.01 (-6.24, -5.77)	14.07
Northeast	-5.89 (-6.07, -5.71)	24.63
Midwest	-5.93 (-6.05, -5.81)	52.50
South	-5.95 (-6.25, -5.65)	8.79
Subtotal (I-squared = 0.0%, p = 0.894)	-5.93 (-6.02, -5.85)	100.00
Heterogeneity between groups: p = 0.000		
Overall (I-squared = 94.7%, p = 0.000)	-5.71 (-5.75, -5.68)	.

8-year physical functioning in the Health Professionals Follow-up Study

Strata	Parameter Estimate (95% CI)	% Weight
Age, years		
<55	-3.36 (-4.07, -2.65)	4.27
55-64	-3.76 (-3.98, -3.54)	43.45
65-74	-3.91 (-4.15, -3.67)	37.72
>=75	-3.97 (-4.35, -3.58)	14.56
Subtotal (I-squared = 0.3%, p = 0.390)	-3.83 (-3.98, -3.68)	100.00
BMI, kg/m^2		
Underweight/Normal, <25.0	-4.95 (-5.18, -4.72)	38.02
Overweight, 25-29.9	-4.88 (-5.09, -4.68)	48.62
Obese, >=30	-4.91 (-5.30, -4.52)	13.36
Subtotal (I-squared = 0.0%, p = 0.909)	-4.91 (-5.05, -4.77)	100.00
Tobacco abuse		
Never	-4.99 (-5.21, -4.77)	44.66
Former	-4.94 (-5.14, -4.73)	51.80
Current	-5.68 (-6.47, -4.89)	3.54
Subtotal (I-squared = 38.2%, p = 0.198)	-4.99 (-5.14, -4.84)	100.00
Race		
White	-5.05 (-5.19, -4.90)	97.17
Non-white	-4.64 (-5.51, -3.78)	2.83
Subtotal (I-squared = 0.0%, p = 0.368)	-5.03 (-5.18, -4.89)	100.00
Region		
West	-5.10 (-5.42, -4.78)	20.31
Northeast	-4.93 (-5.20, -4.67)	29.17
Midwest	-4.74 (-5.01, -4.48)	29.80
South	-5.56 (-5.88, -5.24)	20.72
Subtotal (I-squared = 81.3%, p = 0.001)	-5.04 (-5.18, -4.90)	100.00
Heterogeneity between groups: p = 0.000		
Overall (I-squared = 93.2%, p = 0.000)	-4.76 (-4.83, -4.70)	.

[a] Adjusted for age, race, body mass index, tobacco abuse, and geographic region