

Supplementary Methods

Data source and population

Inclusion criteria included at least three dates on which myeloma diagnostic codes were observed (International Classification of Diseases [ICD]-9: codes with prefix 203.0; ICD-10: codes with prefix C90.0) and at least two dates on which myeloma treatment was observed with the second date falling within six months of the first. The index date on which study follow-up started was the date of the first treatment code, representing the initiation of treatment.

We limited our study to Veterans with an index date falling within the years 2004 through 2017, matching the years of available CMS data at the time of analysis. We restricted our study to Veterans age ≥ 65 years at the index date. To further limit our population to Veterans who were consistently utilizing and being treated within VA (versus Veterans treated partially or wholly outside VA), we required at least one VA non-MM diagnosis or procedure code in each year during the 3 years preceding the index date. To exclude Veterans who had received prior treatment or who were being treated outside VA, we excluded Veterans with one or more MM treatment codes in CMS data prior to or up to six months after the index date. Excluding Veterans who did not routinely use VA or whose myeloma was managed outside VA decreased the missingness of our covariates, since CMS data is more limited than VA data with regards to labs and sociodemographic variables. Increasing missingness of key covariates would have increased the risk of confounding given less robust adjustment. Moreover, excluding these Veterans minimized misclassification of treatment and index date—when the Veteran first initiated treatment for their myeloma within VA.

Modifications to Centers for Medicare and Medicaid Services Chronic Conditions Data Warehouse Algorithms

Using codes from previous studies [1], we added peripheral neuropathy to this list given its prevalence and importance in patients with multiple myeloma. We also combined several similar conditions—e.g., “schizophrenia and other psychotic disorders” and “schizophrenia” were combined into one condition (**Supplementary Table 2**). In addition to a mapping of codes, the Chronic Conditions Warehouse defines algorithms as to the number and type (e.g., inpatient versus outpatient) of CMS claims required to define a chronic condition. We did not use these algorithms, because it was not clear how best to adapt them outside the setting of CMS claims data. Instead, we looked for the presence of at least one matching code in the three years prior to index date to define all conditions.

Additional methods of conducting LCA

To maximize stability of results of LCA, for each potential number of classes we repeated the LCA model fit procedure 50 times starting from random initial parameter estimates and chose the fit that minimized negative log likelihood.

Reference

1. Song X, Wilson KL, Kagan J, et al. Cost of peripheral neuropathy in patients receiving treatment for multiple myeloma: a US administrative claims analysis. *Therapeutic advances in hematology* 2019;10:2040620719839025-2040620719839025.

Supplementary Table 1: Centers for Medicare and Medicaid Services List of Chronic and Potentially Disabling Conditions (based on list from February 2019, the latest version used in the current study).

Other Chronic or Potentially Disabling Conditions	
ADHD, Conduct Disorders, and Hyperkinetic Syndrome	Personality Disorders
Alcohol Use Disorders	Post-Traumatic Stress Disorder (PTSD)
Anxiety Disorders	Pressure and Chronic Ulcers
Autism Spectrum Disorders	Schizophrenia
Bipolar Disorder	Schizophrenia and Other Psychotic Disorders
Cerebral Palsy	Sensory - Blindness and Visual Impairment
Cystic Fibrosis and Other Metabolic Developmental Disorders	Sensory - Deafness and Hearing Impairment
Depressive Disorders	Spina Bifida and Other Congenital Anomalies of the Nervous System
Drug Use Disorders	Spinal Cord Injury
Epilepsy	Tobacco Use
Fibromyalgia, Chronic Pain and Fatigue	Traumatic Brain Injury and Nonpsychotic Mental Disorders due to Brain Damage
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS) *	Viral Hepatitis (General), including: <ul style="list-style-type: none"> • Hepatitis A • Hepatitis B (acute or unspecified) • Hepatitis B (chronic) • Hepatitis C (acute) • Hepatitis C (chronic) • Hepatitis C (unspecified) • Hepatitis D • Hepatitis E
Intellectual Disabilities and Related Conditions	
Learning Disabilities	
Leukemias and Lymphomas	
Liver Disease, Cirrhosis and Other Liver Conditions	

Migraine and Chronic Headache	
Mobility Impairments	
Multiple Sclerosis and Transverse Myelitis	
Muscular Dystrophy	
Obesity	
Opioid Use Disorder	
Other Developmental Delays	
Peripheral Vascular Disease (PVD)	

Supplementary Table 2: Modifications made to Centers for Medicare and Medicaid Services Chronic Conditions Data Warehouse

Original Conditions	Combined Condition Names
Alzheimer's Disease and Related Disorders or Senile Dementia	Alzheimer's Disease and Related Disorders or Senile Dementia
Alzheimer's Disease	
Schizophrenia and Other Psychotic Disorders	Schizophrenia and Other Psychotic Disorders
Schizophrenia	
Intellectual Disabilities and Related Conditions	Intellectual Disabilities and Related Conditions
Learning Disabilities	
Anxiety Disorders	Mood Disorders
Depression	
Depressive Disorders	
Post-Traumatic Stress Disorder or PTSD	
Drug Use Disorders	Drug Use Disorders
Opioid Use Disorder	
Additional Condition	
Peripheral Neuropathy	Not applicable

Supplementary Table 3: Posterior prediction probabilities of five multimorbidity patterns that emerged from latent class analysis

Class	Total Number of Patients in Class	Number of Patients with Class Probability $\geq t$			
		t = 25%	t = 50%	t = 75%	t = 90%
Minimal Comorbidity	1507	1507 (100%)	1448 (96.08%)	1035 (68.68%)	695 (46.12%)
Cardiovascular and Metabolic	1568	1568 (100%)	1492 (95.15%)	987 (62.95%)	565 (36.03%)
Psych and Substance Use Disorders	494	494 (100%)	447 (90.49%)	281 (56.88%)	179 (36.23%)
Chronic Lung Disease	805	805 (100%)	717 (89.07%)	462 (57.39%)	290 (36.02%)
Multisystem Impairment	702	702 (100%)	657 (93.59%)	468 (66.67%)	324 (46.15%)

Supplementary Table 4: Distribution of all chronic conditions by multimorbidity pattern

	Overall	Minimal Comorbidity	Cardiovascular and Metabolic	Psych and Substance Use Disorders	Chronic Lung Disease	Multisystem Impairment
n	5076	1507	1568	494	805	702
Acquired Hypothyroidism (%)	689 (13.6)	101 (6.7)	241 (15.4)	82 (16.6)	110 (13.7)	155 (22.1)
Acute Myocardial Infarction (%)	215 (4.2)	0 (0.0)	77 (4.9)	4 (0.8)	24 (3.0)	110 (15.7)
ADHD Conduct Disorders and Hyperkinetic Syndrome (%)	23 (0.5)	1 (0.1)	0 (0.0)	7 (1.4)	2 (0.2)	13 (1.9)
Alcohol Use Disorders (%)	651 (12.8)	156 (10.4)	105 (6.7)	214 (43.3)	94 (11.7)	82 (11.7)
Alzheimers Disease and Related Disorders or Senile Dementia (%)	369 (7.3)	33 (2.2)	76 (4.8)	92 (18.6)	31 (3.9)	137 (19.5)
Anemia (%)	3687 (72.6)	831 (55.1)	1230 (78.4)	371 (75.1)	615 (76.4)	640 (91.2)
Asthma (%)	396 (7.8)	64 (4.2)	44 (2.8)	27 (5.5)	138 (17.1)	123 (17.5)
Atrial Fibrillation (%)	906 (17.8)	64 (4.2)	331 (21.1)	36 (7.3)	164 (20.4)	311 (44.3)
autismspectrumdisorders (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Benign Prostatic Hyperplasia (%)	2084 (41.1)	485 (32.2)	656 (41.8)	234 (47.4)	333 (41.4)	376 (53.6)
Bipolar Disorder (%)	180 (3.5)	12 (0.8)	2 (0.1)	120 (24.3)	0 (0.0)	46 (6.6)
Cataract (%)	3257 (64.2)	661 (43.9)	1160 (74.0)	310 (62.8)	538 (66.8)	588 (83.8)
Cerebral Palsy (%)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Chronic Kidney Disease (%)	2547 (50.2)	370 (24.6)	967 (61.7)	285 (57.7)	351 (43.6)	574 (81.8)
Chronic Obstructive Pulmonary Disease and Bronchiectasis (%)	1653 (32.6)	141 (9.4)	42 (2.7)	165 (33.4)	805 (100.0)	500 (71.2)

Colorectal Cancer (%)	191 (3.8)	38 (2.5)	80 (5.1)	16 (3.2)	22 (2.7)	35 (5.0)
Cystic Fibrosis and Other Metabolic Developmental Disorders (%)	69 (1.4)	18 (1.2)	20 (1.3)	8 (1.6)	7 (0.9)	16 (2.3)
Diabetes (%)	2074 (40.9)	199 (13.2)	932 (59.4)	209 (42.3)	242 (30.1)	492 (70.1)
Drug Use Disorders (%)	237 (4.7)	37 (2.5)	18 (1.1)	126 (25.5)	13 (1.6)	43 (6.1)
endometrialcancer (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epilepsy (%)	89 (1.8)	12 (0.8)	21 (1.3)	26 (5.3)	8 (1.0)	22 (3.1)
Female/Male Breast Cancer (%)	24 (0.5)	5 (0.3)	6 (0.4)	3 (0.6)	1 (0.1)	9 (1.3)
Fibromyalgia, Chronic Pain, and Fatigue (%)	943 (18.6)	154 (10.2)	245 (15.6)	187 (37.9)	141 (17.5)	216 (30.8)
Glaucoma (%)	1176 (23.2)	227 (15.1)	449 (28.6)	132 (26.7)	156 (19.4)	212 (30.2)
Heart Failure (%)	1162 (22.9)	15 (1.0)	395 (25.2)	42 (8.5)	192 (23.9)	518 (73.8)
Hip Pelvic Fracture (%)	178 (3.5)	30 (2.0)	43 (2.7)	33 (6.7)	25 (3.1)	47 (6.7)
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS) (%)	502 (9.9)	6 (0.4)	0 (0.0)	20 (4.0)	339 (42.1)	137 (19.5)
Hyperlipidemia (%)	3885 (76.5)	891 (59.1)	1375 (87.7)	338 (68.4)	623 (77.4)	658 (93.7)
Hypertension (%)	4487 (88.4)	1077 (71.5)	1548 (98.7)	448 (90.7)	715 (88.8)	699 (99.6)
Intellectual Disabilities and Related Conditions (%)	10 (0.2)	2 (0.1)	0 (0.0)	0 (0.0)	2 (0.2)	6 (0.9)
Ischemic Heart Disease (%)	2204 (43.4)	201 (13.3)	846 (54.0)	126 (25.5)	423 (52.5)	608 (86.6)
Leukemias and Lymphomas (%)	449 (8.8)	126 (8.4)	113 (7.2)	38 (7.7)	65 (8.1)	107 (15.2)
Liver Disease, Cirrhosis and Other Liver	371 (7.3)	64 (4.2)	99 (6.3)	86 (17.4)	34 (4.2)	88 (12.5)

Conditions Except Viral Hepatitis (%)						
Lung Cancer (%)	138 (2.7)	18 (1.2)	24 (1.5)	6 (1.2)	54 (6.7)	36 (5.1)
Migraine and Chronic Headache (%)	103 (2.0)	25 (1.7)	10 (0.6)	34 (6.9)	17 (2.1)	17 (2.4)
Mobility Impairments (%)	180 (3.5)	12 (0.8)	44 (2.8)	28 (5.7)	23 (2.9)	73 (10.4)
Multiple Sclerosis and Transverse Myelitis (%)	22 (0.4)	7 (0.5)	2 (0.1)	0 (0.0)	1 (0.1)	12 (1.7)
Muscular Dystrophy (%)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Obesity (%)	1213 (23.9)	159 (10.6)	502 (32.0)	132 (26.7)	158 (19.6)	262 (37.3)
Osteoporosis (%)	527 (10.4)	121 (8.0)	105 (6.7)	62 (12.6)	108 (13.4)	131 (18.7)
otherdevelopmentaldelays (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral Neuropathy (%)	958 (18.9)	119 (7.9)	301 (19.2)	115 (23.3)	117 (14.5)	306 (43.6)
Peripheral Vascular Disease (%)	905 (17.8)	38 (2.5)	354 (22.6)	62 (12.6)	125 (15.5)	326 (46.4)
Personality Disorders (%)	62 (1.2)	8 (0.5)	0 (0.0)	45 (9.1)	0 (0.0)	9 (1.3)
Pressure and Chronic Ulcers (%)	357 (7.0)	23 (1.5)	105 (6.7)	28 (5.7)	20 (2.5)	181 (25.8)
Prostate Cancer (%)	891 (17.6)	207 (13.7)	312 (19.9)	81 (16.4)	171 (21.2)	120 (17.1)
Rheumatoid Arthritis/Osteoarthritis (%)	2661 (52.4)	600 (39.8)	829 (52.9)	290 (58.7)	423 (52.5)	519 (73.9)
Schizophrenia and Other Psychotic Disorders (%)	272 (5.4)	24 (1.6)	30 (1.9)	97 (19.6)	21 (2.6)	100 (14.2)
Sensory Blindness and Visual Impairment (%)	117 (2.3)	12 (0.8)	42 (2.7)	11 (2.2)	15 (1.9)	37 (5.3)
Sensory Deafness and Hearing Impairment (%)	1690 (33.3)	419 (27.8)	486 (31.0)	181 (36.6)	288 (35.8)	316 (45.0)
Spina Bifida and Other Congenital Anomilies of the Nervous System (%)	36 (0.7)	5 (0.3)	8 (0.5)	3 (0.6)	14 (1.7)	6 (0.9)

Spinal Cord Injury (%)	112 (2.2)	23 (1.5)	29 (1.8)	21 (4.3)	11 (1.4)	28 (4.0)
Stroke Transient Ischemic Attack (%)	583 (11.5)	31 (2.1)	196 (12.5)	56 (11.3)	89 (11.1)	211 (30.1)
Tobacco Use (%)	843 (16.6)	221 (14.7)	108 (6.9)	162 (32.8)	226 (28.1)	126 (17.9)
Traumatic Brain Injury and Non-Psychotic Mental Disorders Due to Brain Damage (%)	35 (0.7)	1 (0.1)	6 (0.4)	11 (2.2)	1 (0.1)	16 (2.3)
Viral Hepatitis (%)	136 (2.7)	24 (1.6)	23 (1.5)	56 (11.3)	10 (1.2)	23 (3.3)
Mood Disorders (%)	1796 (35.4)	370 (24.6)	368 (23.5)	462 (93.5)	198 (24.6)	398 (56.7)

Supplementary Table 5: Baseline characteristics of older Veterans newly treated for multiple myeloma in VA, according to five multimorbidity patterns that emerged from latent class analysis.

	Overall	Minimal Comorbidity	Cardiovascular and Metabolic	Psych and Substance Use Disorders	Chronic Lung Disease	Multisystem Impairment
Total N	5076	1507	1568	494	805	702
Age at Diagnosis (median [IQR])	74.8 [69.6, 80.6]	73.2 [68.6, 78.8]	76.0 [70.4, 81.5]	71.0 [67.7, 76.7]	76.5 [70.6, 81.2]	76.5 [71.3, 82.3]
Age at Diagnosis (Categories [%])						
[65,70)	1400 (27.6)	512 (34.0)	355 (22.6)	215 (43.5)	182 (22.6)	136 (19.4)
[70,75)	1195 (23.5)	381 (25.3)	355 (22.6)	126 (25.5)	166 (20.6)	167 (23.8)
[75,80)	1096 (21.6)	288 (19.1)	370 (23.6)	70 (14.2)	210 (26.1)	158 (22.5)
[80,85)	891 (17.6)	229 (15.2)	301 (19.2)	56 (11.3)	160 (19.9)	145 (20.7)
[85,90)	406 (8.0)	83 (5.5)	147 (9.4)	24 (4.9)	72 (8.9)	80 (11.4)
[90,Inf)	88 (1.7)	14 (0.9)	40 (2.6)	3 (0.6)	15 (1.9)	16 (2.3)
Male (%)	5006 (98.6)	1488 (98.7)	1544 (98.5)	487 (98.6)	797 (99.0)	690 (98.3)
Race (%)						
White	3388 (66.7)	1034 (68.6)	1002 (63.9)	301 (60.9)	572 (71.1)	479 (68.2)
Black	1136 (22.4)	317 (21.0)	387 (24.7)	150 (30.4)	138 (17.1)	144 (20.5)
Other	66 (1.3)	20 (1.3)	19 (1.2)	8 (1.6)	9 (1.1)	10 (1.4)
Missing	486 (9.6)	136 (9.0)	160 (10.2)	35 (7.1)	86 (10.7)	69 (9.8)
Income (mean (SD))	43325.27 (74118.31)	47192.74 (78126.27)	45062.77 (81577.57)	33529.48 (53647.44)	38853.29 (57720.40)	43580.08 (76743.92)
ISS Stage (%)						
ISS 1	523 (10.3)	223 (14.8)	131 (8.4)	64 (13.0)	76 (9.4)	29 (4.1)
ISS 2	958 (18.9)	315 (20.9)	273 (17.4)	101 (20.4)	162 (20.1)	107 (15.2)
ISS 3	641 (12.6)	164 (10.9)	228 (14.5)	68 (13.8)	86 (10.7)	95 (13.5)
Missing	2954 (58.2)	805 (53.4)	936 (59.7)	261 (52.8)	481 (59.8)	471 (67.1)

Calcium \geq 11 mg/dL (%)	161 (3.2)	50 (3.3)	59 (3.8)	15 (3.0)	18 (2.2)	19 (2.7)
Missing	425 (8.4)	148 (9.8)	132 (8.4)	20 (4.0)	66 (8.2)	59 (8.4)
Creatinine > 2 mg/dL (%)	1009 (19.9)	156 (10.4)	392 (25.0)	109 (22.1)	138 (17.1)	214 (30.5)
Missing	350 (6.9)	125 (8.3)	106 (6.8)	18 (3.6)	50 (6.2)	51 (7.3)
Hemoglobin < 10 g/dL(%)	1770 (34.9)	423 (28.1)	615 (39.2)	176 (35.6)	262 (32.5)	294 (41.9)
Missing	349 (6.9)	122 (8.1)	98 (6.2)	18 (3.6)	57 (7.1)	54 (7.7)
Platelet < 150,000/microL (%)	1152 (22.7)	306 (20.3)	368 (23.5)	116 (23.5)	177 (22.0)	185 (26.4)
Missing	636 (12.5)	209 (13.9)	181 (11.5)	55 (11.1)	97 (12.0)	94 (13.4)
Transplantation (%)	152 (3.0)	85 (5.6)	37 (2.4)	17 (3.4)	12 (1.5)	1 (0.1)
Novel Therapy at Induction ^a (%)	4376 (86.2)	1312 (87.1)	1358 (86.6)	434 (87.9)	674 (83.7)	598 (85.2)
Thalidomide (%)	1119 (22.0)	319 (21.2)	338 (21.6)	77 (15.6)	219 (27.2)	166 (23.6)
Lenalidomide (%)	1950 (38.4)	662 (43.9)	591 (37.7)	196 (39.7)	286 (35.5)	215 (30.6)
Bortezomib (%)	2069 (40.8)	590 (39.2)	667 (42.5)	250 (50.6)	275 (34.2)	287 (40.9)
Thalidomide and Bortezomib (%)	75 (1.5)	23 (1.5)	22 (1.4)	10 (2.0)	11 (1.4)	9 (1.3)
Lenalidomide and Bortezomib (%)	671 (13.2)	234 (15.5)	207 (13.2)	81 (16.4)	91 (11.3)	58 (8.3)
Novel Therapy over Lifetime ^b (%)	4716 (92.9)	1424 (94.5)	1468 (93.6)	454 (91.9)	740 (91.9)	630 (89.7)
Thalidomide (%)	1388 (27.3)	413 (27.4)	423 (27.0)	101 (20.4)	257 (31.9)	194 (27.6)
Lenalidomide (%)	3174 (62.5)	1056 (70.1)	1009 (64.3)	312 (63.2)	468 (58.1)	329 (46.9)
Bortezomib (%)	2838 (55.9)	866 (57.5)	905 (57.7)	315 (63.8)	391 (48.6)	361 (51.4)
Thalidomide and Bortezomib (%)	485 (9.6)	168 (11.1)	154 (9.8)	46 (9.3)	68 (8.4)	49 (7.0)
Lenalidomide and Bortezomib (%)	1944 (38.3)	675 (44.8)	623 (39.7)	214 (43.3)	254 (31.6)	178 (25.4)

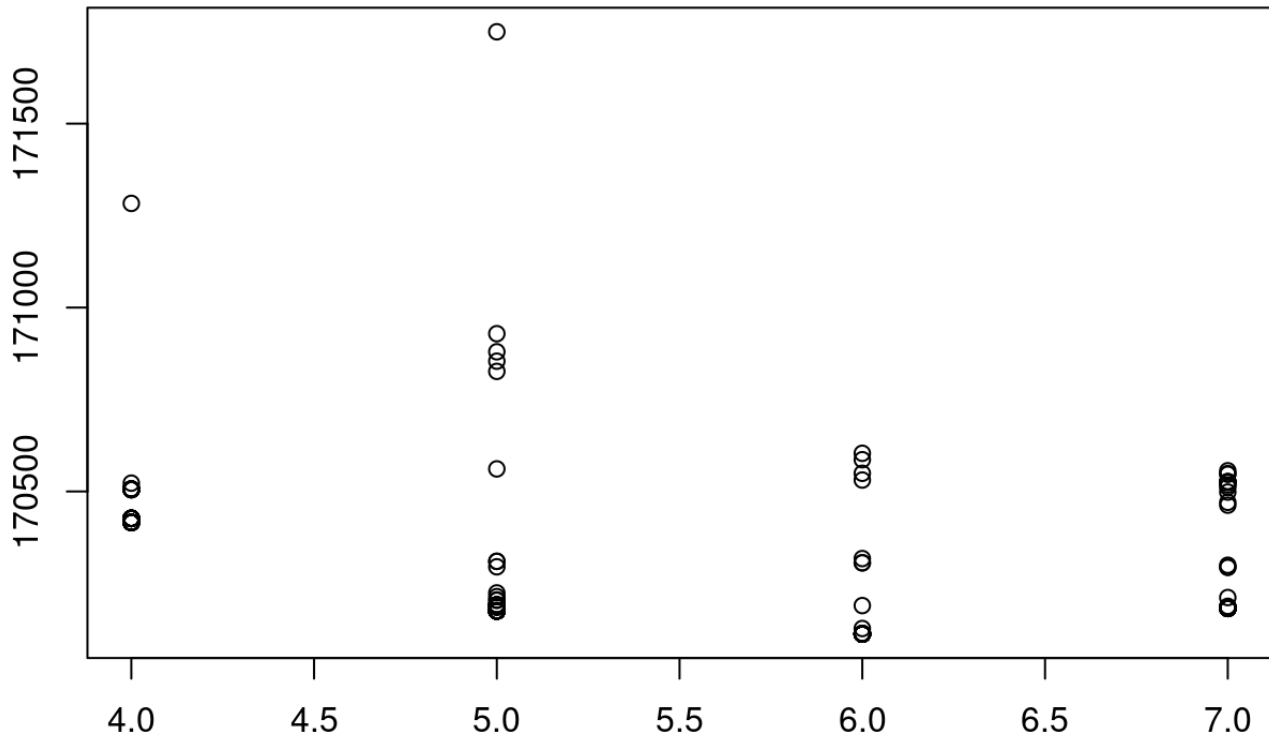
^aTherapy at induction is defined as therapy received in the first 90 days after the index date. Novel therapy is defined to include any proteasome inhibitor (bortezomib, carfilzomib, or ixazomib) or immunomodulatory agent (thalidomide, lenalidomide, or pomalidomide). ^bTherapy over lifetime is defined as therapy received any time during the patient's lifetime. Abbreviations: IQR, interquartile range; ISS, International Staging System

Supplementary Table 6: Complete case analysis involving multivariable Cox proportional hazards regression models estimating effect of multimorbidity patterns on (1) overall mortality, (2) hospitalizations, (3) emergency department (ED) visits^a

Multimorbidity Pattern	Mortality (HR, 95% CI)	ED Visit (HR, 95% CI)	Hospitalization (HR, 95% CI)
Minimal Comorbidity	Reference	Reference	Reference
Cardiovascular and Metabolic	1.01 (0.86 to 1.19)	1.34 (1.15 to 1.56)	1.16 (1.00 to 1.34)
Psych and Substance Use Disorders	1.41 (1.13 to 1.77)	1.72 (1.41 to 2.10)	1.37 (1.12 to 1.67)
Chronic Lung Disease	1.46 (1.21 to 1.76)	1.41 (1.17 to 1.70)	1.51 (1.25 to 1.80)
Multisystem Impairment	1.81 (1.49 to 2.21)	1.65 (1.35 to 2.01)	1.72 (1.42 to 2.09)

^a Models were adjusted for all covariates, including age at MM diagnosis, gender, race, income, ISS stage, calcium \geq 11 mg/dL, creatinine $>$ 2 mg/dL, hemoglobin $<$ 10 g/dL, platelet $<$ 150,000/microL. Abbreviations: ED, emergency department; HR, hazard ratio; CI, confidence interval

Supplementary Figure 1: Model fit (Bayesian Information Criteria [BIC], Y-axis) versus number of classes (X-axis) in the latent class analysis. Each circle represents the BIC for one of the 50 repetitions of the latent class analysis ran for each number of classes.



Supplementary Figure 2: Heat map displaying the probabilities of each condition (rows, labeled along right side) being present conditional upon a Veteran being assigned to each class/multimorbidity pattern (columns, labeled across top). Darker shades indicate a higher probability.

