

SUPPLEMENTAL MATERIAL

Table S1. Cardiovascular Disease (CVD) based on hospital discharge International Classification of Disease 9th and 10th Revisions Clinical Modification (ICD-9/10) codes.

A. Pre-existing CVD

CVD diagnosis	ICD-9 diagnosis codes	ICD-10 diagnosis codes	ICD-9 procedure codes	ICD-10 procedure codes
Prior MI	410.xx, 412.xx	I21.xx, I22.xx, I23.xx, I25.2x	--	--
CAD	410.xx-414.xx, 429.2	I20.xx-I25.xx	--	--
Heart failure	428.x, 402.x1, 404.x1, 404.x3, 398.91	I50.x, I97.13x, I11.0, I13.0, I13.2, I09.81	--	--
Cardiomyopathy	425.1x, 425.4, 425.5, 425.7, 425.8, 425.9, 674.5x	B33.24, E88.89, F10.988, I25.5, I42.1, I42.2, I42.6, I42.7, I42.8, I42.9, I43, O90.3	--	--
HTN	401.xx-405.xx	I10.xx-I15.xx	--	--
CKD	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585.3, 585.4, 585.5, 585.6, 792.5, 996.81, V56.xx	T81.502x, T81.512x, T81.522x, T81.532x, T81.592x, T85.611x, T85.621x, T85.631x, T85.691x, T85.71x, I12.0, I13.11, I13.2, I95.3	--	--

		N18.3, N18.4, N18.5, N18.6, R88.0, T86.1x, Y84.1, Z48.22, Z49.xx, Z91.15, Z94.0, Z99.2		
SVT	427.0	I47.1	--	--
Atrial fibrillation/flutter	427.3x	I48.x	--	--
VT	427.1, 427.4x, 427.5	I46.2, I46.8, I46.9, I47.0, I47.2, I49.0x	--	--
Hyperlipidemia	272.0, 272.1, 272.2, 272.4	E78.0x, E78.1, E78.2, E78.4, E78.5	--	--
Obesity	278.00, 278.01, 278.03, V85.3x, V85.4x	E66.1, E66.2, E66.8, E66.9, E66.0x, Z68.3x, Z68.4x	--	--
Diabetes mellitus (Defined as either 2 outpatient visits with diagnoses codes or 1 inpatient stay with diagnoses codes)	250.xx, 362.0x, 357.2, 366.41	E08.xx, E09.xx, E10.xx, E11.xx, E13.xx	--	--
Stroke	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436, 444	I63.x, I74.x	--	--

Prior PCI	V45.82	Z98.61, Z95.5	00.66, 36.0x CPT codes: 92920, 92921, 92924, 92925, 92928, 92929, 92933, 92934, 92937, 92938, 92941, 92943, 92944, 92980, 92981, 92982, 92984, 92995, 92996, 92975, 92977	0270x, 0271x, 0272x, 0273x, 02C0, 02C1, 02C2, 02C3
Prior CABG	V45.81, 414.02, 414.03, 414.04, 414.05	I25.810, I25.812, Z95.1, T82.21, I25.7x except I25.75x	36.1x CPT codes: 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33533, 33534, 33535, 33536 HCPC: 4110F	02100x, 02110x, 02120x, 02130x
Prior valve replacement	--	--	35.24, 35.22, 35.26, 35.28, 35.23, 35.21, 35.25, 35.27,	02RG0JZ, 02RF0JZ, 02RH0JZ,

			35.12, 35.11, 35.13, 35.14, 35.33, 35.05, 35.06, 35.07, 35.08, 35.09, 35.96, 35.97, 35.00, 35.01, 35.02, 35.03, 35.04 CPT codes: 33405, 33430, 33406, 33410, 33411, 33412, 33413, 33465, 33475, 33422, 33425, 33426, 33427, 33400, 33401, 33403, 33864, 33460, 33464, 33474, 33417, 33468, 33496, 33600, 33602, 33418, 33419, 33361, 33362, 33363, 33364, 33365, 33366, 33367, 33368, 33369, 33420, 33470, 33471, 33477, 92987	02RJ0JZ, 02RG07Z, 02RG08Z, 02RG0KZ, 02RF07Z, 02RF08Z, 02RF0KZ, 02RH07Z, 02RH08Z, 02RH0KZ, 02RJ07Z, 02RJ08Z, 02RJ0KZ, 027G04Z, 027G0DZ, 027G0ZZ, 02NG0ZZ, 02QG0ZZ, 02CG0ZZ, 02UG0JZ, 027F0ZZ, 02NF0ZZ, 02QF0ZZ, 02UF0JZ, 027H0ZZ, 02NH0ZZ, 02QH0ZZ, 027J0ZZ, 02NJ0ZZ, 02QJ0ZZ, 02UH0JZ, 02UJ0JZ,
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			HCPC codes: 0257T, 0258T, 0259T, 0262T, 0318T	02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, 02RF3KZ, 02RF47Z, 02RF48Z, 02RF4KZ, 02RG37H, 02RG37Z, 02RG38H, 02RG38Z, 02RG3JH, 02RG3KH, 02RG3KZ, 02RG47Z, 02RG48Z, 02RG4KZ, 02RH37H, 02RH37Z, 02RH38H, 02RH38Z, 02RH3JH, 02RH3JZ, 02RH3KH, 02RH3KZ, 02RH47Z, 02RH48Z, 02RH4KZ,
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				02RJ47Z, 02RJ48Z, 02RJ4KZ, X2RF332, 027F3ZZ, 027G3ZZ, 027H3ZZ, 027J3ZZ, 02CF3ZZ, 02CF4ZZ, 02CG3ZZ, 02CG4ZZ, 02CH3ZZ, 02CH4ZZ, 02CJ3ZZ, 02CJ4ZZ, 02NF3ZZ, 02NF4ZZ, 02NG3ZZ, 02NG4ZZ, 02NH3ZZ, 02NH4ZZ, 02NJ3ZZ, 02NJ4ZZ, 02UG3JZ
Prior ICD/PPM	V53.31, V45.00, V45.01, 996.01, 996.61, V45.02	Z95.0, Z45.0x, Z95.810	37.71, 37.75, 37.76, 37.79, 37.80, 37.81, 37.82, 37.85, 37.86, 37.89, 39.64, 89.45, 89.46, 89.47,	02HK0JZ, 02HK3JZ, 02HK4JZ, 02HK0MZ, 02HK3MZ, 02HK4MZ, 02HK0NZ,

		<p>89.48, 37.70, 37.72, 37.73, 37.83, 37.87, 37.20, 37.94, 37.95, 37.96, 37.97, 37.98, 89.49, 00.50, 00.51, 00.52, 00.53, 00.54</p> <p>CPT codes: 33216, 33207, 33212, 33218, 33222, 33224, 33225, 33227, 33233, 93279, 93286, 93288, 93293, 93294, 93296, 93724, 33217, 33206, 33208, 33213, 33221, 93280, 93281, 33228, 33229, 33220, 33214, 33215, 33223, 33230, 33231, 33240, 33241, 33249, 33262, 33263, 33264, 93260, 93261, 93282, 93283, 93284,</p>	<p>02HK3NZ, 02HK4NZ, 0JH804Z, 0JH834Z, 0JH604Z, 0JH634Z, 0JH805Z, 0JH835Z, 0JH605Z, 0JH635Z, 4B02XSZ, 02WA0NZ, 02WA3NZ, 02WA4NZ, 02WA0MZ, 02WA3MZ, 02WA4MZ, 02H60JZ, 02H63JZ, 02H64JZ, 02H60MZ, 02H63MZ, 02H64MZ, 02H60NZ, 02H63NZ, 02H64NZ, 0JH806Z, 0JH836Z, 0JH606Z, 0JH636Z, 0JH808Z, 0JH838Z, 0JH608Z,</p>
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			93287, 93289, 93295, 33226 HCPC codes: 0389T, 0390T, 0391T	0JH638Z, 02H40KZ, 02H43KZ, 02H44KZ, 02H70KZ, 02H73KZ, 02H74KZ, 02HL0K, 02HL3KZ, 02HL4KZ, 02HN0KZ, 02HN3KZ, 02HN4KZ, 02H60K, 02H63KZ, 02H64K, 02HK0KZ, 02HK3KZ, 02HK4KZ, 4B02XTZ, 0JH807Z, 0JH837Z, 0JH607Z, 0JH637Z, 02H40NZ, 02H43NZ, 02H44NZ, 02H40JZ, 02H43JZ, 02H44JZ, 02HN0JZ, 02HN3JZ, 02HN4JZ
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Prior dialysis	--	--	39.95, 54.98 CPT codes: 90935, 90937, 90940, 90965, 90966, S9335, 99512, 90945, 90947, 90969, 90970, 90999, G0257	5A1D00Z, 5A1D60Z, 3E1M39Z Revenue codes: 0820-0829, 0800, 0802-0809, 0830- 0859, 0880-0889
History of smoking	V15.82, 649.0x, 305.1, 989.84	F17.xxx, O99.33x, T65.2x, Z53.01, Z71.6, Z72.0, Z87.891	CPT codes: 1034F, 4000F, 4001F, 4004F, 99406, 99407, C9801, C9802, D1320, G0375, G0376, G0436, G0437, G8402, G8453, G8455, G9276, G9458, G9792	--
Active smoking (i.e. documented within 30 days prior to index hospitalization)	649.0x, 305.1, 989.84	F17.xxx, O99.33x, Z53.01, Z72.0	--	--

B. CVD during index hospitalization

Diagnosis	ICD-9 codes	ICD-10 codes
Heart failure	428.x, 402.x1, 404.x1, 404.x3, 398.91	I50.x, I97.13x, I11.0, I13.0, I13.2, I09.81

Acute MI	410.x1	I21.x
Unstable angina	411.1	I20.0, I25.110, I25.700, I25.710, I25.720, I25.730, I25.750, I25.760, I25.790
Atrial fibrillation or flutter	427.3x	I48.x
Cardiac arrest / VF	427.4x, 427.5	I46.x, I49.0x
Cardiogenic shock	785.51	R57.0
Coronary disease	414.x (except 414.1x)	I25.1x, I25.7x, I25.8x, I25.9
Valve disease of any type	424.0-3, 394.x, 396.x, 746.6	I05-I08.x, I34-I37.x, Q23.3
Cardiomyopathy	425.1x, 425.4, 425.5, 425.7, 425.8, 425.9, 674.5x	B33.24, E88.89, F10.988, I25.5, I42.1, I42.2, I42.6, I42.7, I42.8, I42.9, I43, O90.3
SVT other than AF	427.0	I47.1
VT other than VF	427.1, 427.4x, 427.5	I46.2, I46.8, I46.9, I47.0, I47.2, I49.0x
Ischemic Stroke/systemic embolism	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 436, 444	I63.x, I74.x
Intracranial hemorrhage	430, 431, 432.x, 852.x, 853.x, 800.2x, 800.3x, 800.7x, 800.8x, 801.2x, 801.3x, 801.7x, 801.8x, 803.2x, 803.3x, 803.7x, 803.8x, 804.2x, 804.3x, 804.7x, 804.8x	I60.x, I61.x, S06.34x, S06.35x, S06.36x, S06.37x, S06.38x, S06.4x, S06.5x, S06.6x

Table S2. Cardiovascular Risk Factors based on hospital discharge International Classification of Disease 9th and 10th Revisions Clinical Modification (ICD-9/10) codes.

Risk Factor	ICD-9 diagnosis codes	ICD-10 diagnosis codes
Hypertension	401.xx-405.xx	I10.xx-I15.xx
Hyperlipidemia	272.0, 272.1, 272.2, 272.4	E78.0x, E78.1, E78.2, E78.4, E78.5
Diabetes mellitus	250.xx, 362.0x, 357.2, 366.41	E08.xx, E09.xx, E10.xx, E11.xx, E13.xx
Chronic kidney disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585.3, 585.4, 585.5, 585.6, 792.5, 996.81, V56.xx	T81.502x, T81.512x, T81.522x, T81.532x, T81.592x, T85.611x, T85.621x, T85.631x, T85.691x, T85.71x, I12.0, I13.11, I13.2, I95.3, N18.3, N18.4, N18.5, N18.6, R88.0, T86.1x, Y84.1, Z48.22, Z49.xx, Z91.15, Z94.0, Z99.2
Obesity	278.00, 278.01, 278.03, V85.3x, V85.4x	E66.1, E66.2, E66.8, E66.9, E66.0x, Z68.3x, Z68.4x
Tobacco dependence	649.0x, 305.1, 989.84	F17.xxx, O99.33x, Z53.01, Z72.0

Table S3. Explicit Sepsis Definition based on hospital discharge International Classification of Disease 9th and 10th Revisions Clinical Modification (ICD-9/10) codes.

Diagnosis	ICD-9 diagnosis codes	ICD-10 diagnosis codes
Sepsis	995.9x, 038.x, 790.7, 020.0, 112.5, 112.81 117.9	A40.x, A41.x, R65.1x, R65.20, R78.81, A02.1, A20.7, A22.7, A26.7, A32.7, A42.7, B37.7
Septic shock	785.52	R65.21

Table S4. Implicit Sepsis Definition based on hospital discharge International Classification of Disease 9th and 10th Revisions Clinical Modification (ICD-9/10) codes. Implicit sepsis required at least one ICD-9/10 code for infection (A) and at least one ICD-9/10 code for organ dysfunction.

A. Infection

Diagnosis	ICD-9 diagnosis codes	ICD-10 diagnosis codes
Bacterial/fungal infections	001-005, 008-018, 020-027, 031-041, 090-098, 100-104, 110-112, 114-118	A00-05, A09, A15, A17-19, A20-28, A30-32, A35-49, A50-54, A65-69, B35-49, B95-96
CNS	320, 322, 324, 325	G00, G01, G06, G08
Cardiac/vascular	420, 421, 451	I30, I33, I80
ENT/URI	461-465	J01-04, J06
Pulmonary	481, 482, 485, 586, 491.21, 494, 510, 513	J13, J14, J15, J18, J95.81x, J69.0, J47, J44.0, J86, J85
GI	540-542, 562.01/03, 562.11/13, 566, 567, 569.5, 569.83, 572.0, 572.1, 575.0	K35-37, K57.0x, K57.2x, K57.4x, K57.8x, K57.92, K57.93, K61, K65, K63.1, K63.0, K75.0, K75.1, K81.0, K81.2
GU	590, 597, 599.0, 601, 614-616	N10, N39.0, N34, N41, N70-73
Skin/soft tissue/bone/joint	681-683, 686, 711.0, 730, 785.4, 728.86	I96, M72.6, L03-04, L08, M00, M86,
Iatrogenic	998.5, 999.3	T81.4x, T82.6x, T82.7x, T83.5x, T83.6x, T84.5x, T84.6x, T84.7x, T85.7x, T87.5x, T88.0x, T80.2x
Sepsis/bacteremia	995.9x, 790.7, 785.52	R65.1x, R65.2x R78.81, T81.12x

B. Organ dysfunction

Diagnosis	ICD-9 diagnosis codes	ICD-10 diagnosis codes	ICD-9 procedure codes	ICD-10 procedure codes
Respiratory failure	518.81, 518.82, 518.85, 786.09, 799.1	J96.0x, J96.2x, J96.9x, R06.03, R09.2	96.7x	5A1935Z 5A1945Z 5A1955Z
Circulatory failure	458.x, 785.5x, 796.3	R57.9, I95.x, R65.21	---	---
Renal failure	584.x, 580.x	N00.x, N17.x	39.95	5A1D70Z 5A1D80Z 5A1D90Z
Hepatic failure	570, 572.2, 573.3	K72.0x, K72.9x, K75.9	---	---
Hematologic failure	286.2, 286.6, 286.9, 287.3x, 287.4x, 287.5	D65, D69.5x, D69.6, D68.9	---	---
Metabolic failure	276.2	E87.2	---	---
Neurologic failure	293.xx, 348.1, 348.3x, 780.01, 780.09	G92, G93.4x, G93.1, F05, R41.0, F06.0, F06.2, R40.20, R40.4, R40.1, R41.82	89.14	4A00x4Z where x=3,7,8,X 4A01x4Z where x=3,7,8,X 4A10x4Z where x=3,7,8,X 4A11x4Z where x=3,7,8,X

Table S5. Index Hospitalization Characteristics based on hospital discharge International Classification of Disease 9th and 10th Revisions Clinical Modification (ICD-9/10) codes.

Characteristic	ICD-9 diagnosis codes	ICD-10 diagnosis codes	ICD-9 procedure codes	ICD-10 procedure codes
Infection	See Supplementary Table 2A		--	--
Organ failure	See Supplementary Table 2B		--	--
Intensive care unit	Revenue codes: 020x, 021x		--	--
Invasive ventilation	--	--	96.70, 96.71, 96.72	5A1935Z, 5A1945Z, 5A1955Z
Hemodialysis	--	--	39.95	5A1D70Z, 5A1D80Z, 5A1D90Z
CVD diagnosis	See Supplementary Table 3B		--	--

Table S6: Variables included in the propensity score for sepsis and standard mean differences between the sepsis and no sepsis groups before and after propensity score overlap weighting.

	Before Propensity Score Weighting			After Propensity Score Weighting		
	No sepsis (N=1,449,821)	Sepsis (N=808,673)	Standardized Difference	No sepsis (N=1,449,821)	Sepsis (N=808,673)	Standardized Difference
Age group						
18-54 years	450919 (31.1%)	124249 (15.4%)	0.379	21.2%	21.2%	0.000
55-64 years	347422 (24.0%)	158929 (19.7%)	0.105	22.1%	22.1%	0.000
65-74 years	285200 (19.7%)	194439 (24.0%)	0.106	22.3%	22.3%	0.000
75+ years	366280 (25.3%)	331056 (40.9%)	0.338	34.3%	34.3%	0.000
Sex						
Female	789512 (54.5%)	438058 (54.2%)	0.006	55.5%	55.5%	0.000
Male	660309 (45.5%)	370615 (45.8%)	0.006	44.5%	44.5%	0.000
Race						
Unknown	251601 (17.4%)	103265 (12.8%)	0.128	14.8%	14.8%	0.000
Asian	29042 (2.0%)	15110 (1.9%)	0.010	1.8%	1.8%	0.000
Black	175974 (12.1%)	111714 (13.8%)	0.050	13.0%	13.0%	0.000
Hispanic	104386 (7.2%)	56237 (7.0%)	0.010	7.3%	7.3%	0.000
White	888818 (61.3%)	522347 (64.6%)	0.068	63.1%	63.1%	0.000
Region						
Unknown	3055 (0.2%)	1186 (0.1%)	0.015	0.2%	0.2%	0.000
Midwest	404171 (27.9%)	226434 (28.0%)	0.003	27.5%	27.5%	0.000
Northeast	227047 (15.7%)	132902 (16.4%)	0.021	16.1%	16.1%	0.000
South	666092 (45.9%)	368145 (45.5%)	0.008	46.4%	46.4%	0.000
West	149456 (10.3%)	80006 (9.9%)	0.014	9.8%	9.8%	0.000
Health plan						

Commercial	789400 (54.4%)	257979 (31.9%)	0.467	41.4%	41.4%	0.000
Medicare Advantage	660421 (45.6%)	550694 (68.1%)	0.467	58.6%	58.6%	0.000
Pharmacy coverage	992543 (68.5%)	604885 (74.8%)	0.141	72.0%	72.0%	0.000
Infection type						
Bacteria/fungal	83972 (5.8%)	381206 (47.1%)	1.061	31.2%	31.2%	0.000
CNS	2621 (0.2%)	3769 (0.5%)	0.050	0.4%	0.4%	0.000
Cardiovascular	9231 (0.6%)	11786 (1.5%)	0.081	1.6%	1.6%	0.000
ENT/URI	14039 (1.0%)	15748 (1.9%)	0.082	2.6%	2.6%	0.000
Pulmonary	68570 (4.7%)	277549 (34.3%)	0.805	17.0%	17.0%	0.000
GI	52010 (3.6%)	31670 (3.9%)	0.017	5.9%	5.9%	0.000
GU	81736 (5.6%)	247626 (30.6%)	0.686	23.2%	23.2%	0.000
Skin/soft tissue/bone/joint	73925 (5.1%)	82120 (10.2%)	0.191	14.3%	14.3%	0.000
Iatrogenic	14444 (1.0%)	21269 (2.6%)	0.123	3.2%	3.2%	0.000
Sepsis/bacteremia	3242 (0.2%)	168363 (20.8%)	0.713	2.3%	2.3%	0.000
Organ failure type						
Respiratory	85496 (5.9%)	258185 (31.9%)	0.705	14.9%	14.9%	0.000
Circulatory	61094 (4.2%)	138130 (17.1%)	0.427	9.9%	9.9%	0.000
Renal	136693 (9.4%)	338870 (41.9%)	0.801	24.1%	24.1%	0.000
Hepatic	8512 (0.6%)	17715 (2.2%)	0.137	1.6%	1.6%	0.000
Hematologic	42621 (2.9%)	81473 (10.1%)	0.292	7.2%	7.2%	0.000
Metabolic	26155 (1.8%)	53766 (6.6%)	0.243	4.3%	4.3%	0.000
Neurologic	76993 (5.3%)	179734 (22.2%)	0.506	12.7%	12.7%	0.000
Comorbidities						
MI	133617 (9.2%)	126051 (15.6%)	0.194	11.9%	11.9%	0.000
CAD	446032 (30.8%)	356481 (44.1%)	0.278	37.1%	37.1%	0.000

Heart failure	222407 (15.3%)	256655 (31.7%)	0.394	23.0%	23.0%	0.000
Cardiomyopathy	100189 (6.9%)	96784 (12.0%)	0.174	9.0%	9.0%	0.000
Hypertension	1069012 (73.7%)	691060 (85.5%)	0.294	80.8%	80.8%	0.000
Chronic kidney disease	121454 (8.4%)	162920 (20.1%)	0.341	14.1%	14.1%	0.000
SVT	47782 (3.3%)	37337 (4.6%)	0.068	3.7%	3.7%	0.000
Atrial fibrillation/flutter	203769 (14.1%)	189976 (23.5%)	0.243	18.0%	18.0%	0.000
VT	48135 (3.3%)	47666 (5.9%)	0.123	4.3%	4.3%	0.000
Hyperlipidemia	1010638 (69.7%)	621013 (76.8%)	0.161	73.7%	73.7%	0.000
Obesity	394056 (27.2%)	248730 (30.8%)	0.079	29.5%	29.5%	0.000
Diabetes	440949 (30.4%)	352441 (43.6%)	0.275	38.1%	38.1%	0.000
Stroke	133088 (9.2%)	138394 (17.1%)	0.236	12.6%	12.6%	0.000
PCI	103615 (7.1%)	80653 (10.0%)	0.101	8.1%	8.1%	0.000
CABG	85075 (5.9%)	73615 (9.1%)	0.123	7.3%	7.3%	0.000
Valve procedure	11597 (0.8%)	10459 (1.3%)	0.049	1.0%	1.0%	0.000
ICD/PPM	69439 (4.8%)	65183 (8.1%)	0.134	6.3%	6.3%	0.000
Renal failure requiring dialysis	17198 (1.2%)	26182 (3.2%)	0.140	2.1%	2.1%	0.000
History of smoking	456169 (31.5%)	321588 (39.8%)	0.174	35.0%	35.0%	0.000
Active smoker	296008 (20.4%)	189433 (23.4%)	0.073	21.3%	21.3%	0.000
Index hospitalization						
ICU	449257 (31.0%)	357378 (44.2%)	0.275	32.9%	32.9%	0.000
Invasive ventilation	11580 (0.8%)	41662 (5.2%)	0.258	2.2%	2.2%	0.000
Hemodialysis	4625 (0.3%)	17447 (2.2%)	0.167	1.0%	1.0%	0.000
CV diagnosis						
Heart failure	204613 (14.1%)	225294 (27.9%)	0.342	19.7%	19.7%	0.000
MI	55056 (3.8%)	41637 (5.1%)	0.065	3.6%	3.6%	0.000
Angina	37072 (2.6%)	8435 (1.0%)	0.114	1.2%	1.2%	0.000
Atrial fibrillation	207768 (14.3%)	168809 (20.9%)	0.172	16.2%	16.2%	0.000
Cardiac arrest	5626 (0.4%)	6974 (0.9%)	0.060	0.5%	0.5%	0.000
Cardiogenic shock	1732 (0.1%)	4615 (0.6%)	0.077	0.3%	0.3%	0.000

CAD	267646 (18.5%)	167828 (20.8%)	0.058	19.0%	19.0%	0.000
Valve disease	176252 (12.2%)	124402 (15.4%)	0.094	12.9%	12.9%	0.000
Cardiomyopathy	76338 (5.3%)	54715 (6.8%)	0.063	5.5%	5.5%	0.000
SVT	19657 (1.4%)	15716 (1.9%)	0.046	1.5%	1.5%	0.000
VT	27752 (1.9%)	23518 (2.9%)	0.065	2.1%	2.1%	0.000
Stroke	133127 (9.2%)	60554 (7.5%)	0.061	7.0%	7.0%	0.000
Intracranial bleeding	36876 (2.5%)	12669 (1.6%)	0.069	1.7%	1.7%	0.000

Table S7: 30-day event rates (per 100 patients) in patients with and without sepsis, as a function of sepsis group.

	No Sepsis (ref)			Sepsis		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes	N=1,449,821			N=808,673		
Mortality	3,329	1,449,821	0.23	6,355	808,673	0.79
All-cause hospitalization	103,387	1,446,672	7.15	95,608	802,667	11.91
CVD hospitalization	34,934	1,446,672	2.41	38,569	802,667	4.81
Composite #1	106,382	1,446,672	7.35	101,565	802,667	12.65
Composite #2	38,122	1,446,672	2.64	44,741	802,667	5.57
	No Sepsis (ref)			Implicit Sepsis Only		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes	N=1,449,821			N=448,644		
Mortality	3,329	1,449,821	0.23	2,750	448,644	0.61
All-cause hospitalization	103,387	1,446,672	7.15	56,465	446,062	12.66
CVD hospitalization	34,934	1,446,672	2.41	24,813	446,062	5.56
Composite #1	106,382	1,446,672	7.35	58,973	446,062	13.22
Composite #2	38,122	1,446,672	2.64	27,446	446,062	6.15
	No Sepsis (ref)			Explicit Sepsis Only		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes	N=1,449,821			N=124,841		
Mortality	3,329	1,449,821	0.23	247	124,841	0.20
All-cause hospitalization	103,387	1,446,672	7.15	12,399	124,612	9.95
CVD hospitalization	34,934	1,446,672	2.41	3,393	124,612	2.72
Composite #1	106,382	1,446,672	7.35	12,599	124,612	10.11
Composite #2	38,122	1,446,672	2.64	3,625	124,612	2.91

	No Sepsis (ref)			Both Sepsis Types		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes		N=1,449,821			N=235,188	
Mortality	3,329	1,449,821	0.23	3,358	235,188	1.43
All-cause hospitalization	103,387	1,446,672	7.15	26,744	231,993	11.53
CVD hospitalization	34,934	1,446,672	2.41	10,363	231,993	4.47
Composite #1	106,382	1,446,672	7.35	29,993	231,993	12.93
Composite #2	38,122	1,446,672	2.64	13,670	231,993	5.89

Table S8: 90-day event rates (per 100 patients) in patients with and without sepsis, as a function of sepsis group.

	No Sepsis (ref)			Sepsis		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes	N=1,449,821			N=808,673		
Mortality	38,419	1,449,821	2.65	54,776	808,673	6.77
All-cause hospitalization	211,510	1,341,267	15.77	212,135	718,898	29.51
CVD hospitalization	74,867	1,341,267	5.58	92,702	718,898	12.90
Composite #1	235,200	1,341,267	17.54	242,744	718,898	33.77
Composite #2	106,018	1,341,267	7.90	134,079	718,898	18.65
	No Sepsis (ref)			Implicit Sepsis Only		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes	N=1,449,821			N=448,644		
Mortality	38,419	1,449,821	2.65	31,314	448,644	6.98
All-cause hospitalization	211,510	1,341,267	15.77	124,503	397,909	31.29
CVD hospitalization	74,867	1,341,267	5.58	58,801	397,909	14.78
Composite #1	235,200	1,341,267	17.54	140,995	397,909	35.43
Composite #2	106,018	1,341,267	7.90	81,522	397,909	20.49
	No Sepsis (ref)			Explicit Sepsis Only		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes	N=1,449,821			N=124,841		
Mortality	38,419	1,449,821	2.65	4,067	124,841	3.26
All-cause hospitalization	211,510	1,341,267	15.77	26,588	115,517	23.02
CVD hospitalization	74,867	1,341,267	5.58	8,115	115,517	7.02
Composite #1	235,200	1,341,267	17.54	28,583	115,517	24.74
Composite #2	106,018	1,341,267	7.90	11,270	115,517	9.76
	No Sepsis (ref)			Both Sepsis Types		

	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes		N=1,449,821			N=235,188	
Mortality	38,419	1,449,821	2.65	19,395	235,188	8.25
All-cause hospitalization	211,510	1,341,267	15.77	61,044	205,472	29.71
CVD hospitalization	74,867	1,341,267	5.58	25,786	205,472	12.55
Composite #1	235,200	1,341,267	17.54	73,166	205,472	35.61
Composite #2	106,018	1,341,267	7.90	41,287	205,472	20.09

Table S9: One-year event rates (per 100 patients) in patients with and without sepsis, as a function of sepsis group.

	No Sepsis (ref)			Sepsis		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes		N=1,449,821			N=808,673	
Mortality	98,865	1,449,821	6.82	133,624	808,673	16.52
All-cause hospitalization	395,079	1,027,742	38.44	367,434	524,886	70.00
CVD hospitalization	151,195	1,027,742	14.71	178,674	524,886	34.04
Composite #1	440,830	1,027,742	42.89	416,748	524,886	79.40
Composite #2	221,919	1,027,742	21.59	261,390	524,886	49.80
	No Sepsis (ref)			Implicit Sepsis Only		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes		N=1,449,821			N=448,644	
Mortality	98,865	1,449,821	6.82	79,888	448,644	17.81
All-cause hospitalization	395,079	1,027,742	38.44	216,632	286,201	75.69
CVD hospitalization	151,195	1,027,742	14.71	112,965	286,201	39.47
Composite #1	440,830	1,027,742	42.89	244,546	286,201	85.45
Composite #2	221,919	1,027,742	21.59	160,111	286,201	55.94
	No Sepsis (ref)			Explicit Sepsis Only		
	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes		N=1,449,821			N=124,841	
Mortality	98,865	1,449,821	6.82	11,621	124,841	9.31
All-cause hospitalization	395,079	1,027,742	38.44	47,176	88,898	53.07
CVD hospitalization	151,195	1,027,742	14.71	17,100	88,898	19.24
Composite #1	440,830	1,027,742	42.89	50,940	88,898	57.30
Composite #2	221,919	1,027,742	21.59	24,836	88,898	27.94
	No Sepsis (ref)			Both Sepsis Types		

	No. with Events	No. of Enrollees	Event Rate per 100	No. with Events	No. of Enrollees	Event Rate per 100
Outcomes		N=1,449,821			N=235,188	
Mortality	98,865	1,449,821	6.82	42,115	235,188	17.91
All-cause hospitalization	395,079	1,027,742	38.44	103,626	149,787	69.18
CVD hospitalization	151,195	1,027,742	14.71	48,599	149,787	32.45
Composite #1	440,830	1,027,742	42.89	121,262	149,787	80.96
Composite #2	221,919	1,027,742	21.59	76,443	149,787	51.03

Table S10: Risk of all-cause post-discharge mortality associated with sepsis (all definitions) across subgroups. P values for interaction are unadjusted.

	No Sepsis (ref)			Sepsis			Hazard Ratio (95% CI)	P Value	P Value for interaction
	No. with Events	Person Years	Event Rate per 100	No. with Events	Person Years	Event Rate per 100			
Age group									<0.0001
All <65 years	25,610	2,127,816	1.20	31,370	646,525	4.85	1.83 (1.77, 1.90)	<0.0001	
65+ years	141,883	1,573,707	9.02	189,058	1,048,002	18.04	1.22 (1.20, 1.23)	<0.0001	
50-64 years	21,442	1,306,173	1.64	26,855	471,293	5.70	1.87 (1.80, 1.94)	<0.0001	
<50 years	4,168	821,643	0.51	4,515	175,232	2.58	2.04 (1.86, 2.23)	<0.0001	
Sex									0.0001
Male	81,297	1,641,434	4.95	104,053	755,290	13.78	1.28 (1.25, 1.30)	<0.0001	
Female	86,196	2,060,089	4.18	116,375	939,237	12.39	1.26 (1.24, 1.28)	<0.0001	
Race/Ethnicity									<0.0001
Asian	2,910	76,916	3.78	3,910	32,400	12.07	1.28 (1.16, 1.42)	<0.0001	
Black	21,512	426,475	5.04	32,457	225,903	14.37	1.31 (1.26, 1.36)	<0.0001	
Hispanic	8,382	261,598	3.20	12,216	115,521	10.57	1.32 (1.25, 1.40)	<0.0001	
White	120,942	2,287,774	5.29	155,325	1,113,655	13.95	1.23 (1.21, 1.25)	<0.0001	
All non-White	46,551	1,413,750	3.29	65,103	580,872	11.21	1.37 (1.34, 1.41)	<0.0001	
Health plan									<0.0001
Commercial	23,033	2,055,952	1.12	22,546	564,867	3.99	1.82 (1.75, 1.89)	<0.0001	
Medicare Advantage	144,460	1,645,572	8.78	197,882	1,129,660	17.52	1.21 (1.19, 1.22)	<0.0001	
Pharmacy coverage									<0.0001
No	43,648	1,271,498	3.43	47,650	457,007	10.43	1.26 (1.22, 1.29)	<0.0001	
Yes	123,845	2,430,026	5.10	172,868	1,237,520	13.97	1.27 (1.25, 1.29)	<0.0001	
Prior CVD									<0.0001
No	56,704	2,153,457	2.63	53,264	724,153	7.36	1.35 (1.32, 1.38)	<0.0001	
Yes	110,789	1,548,067	7.16	167,164	970,374	17.23	1.21 (1.19, 1.23)	<0.0001	
# of CVD risk factors									<0.0001
<3	74,282	2,066,007	3.60	69,862	653,848	10.68	1.25 (1.22, 1.27)	<0.0001	
3+	93,211	1,635,516	5.70	150,566	1,040,680	14.47	1.28 (1.26, 1.30)	<0.0001	
ICU during index hospitalization									<0.0001
No	112,668	2,589,391	4.35	118,549	976,556	12.14	1.26 (1.24, 1.28)	<0.0001	
Yes	54,825	1,112,133	4.93	101,879	717,971	14.19	1.19 (1.16, 1.22)	<0.0001	

CVD diagnosis during index hospitalization										0.0183
No	62,629	2,123,764	2.95	68,723	808,795	8.50	1.42 (1.39, 1.45)	<0.0001		
Yes	104,864	1,577,759	6.65	151,705	885,732	17.13	1.14 (1.12, 1.16)	<0.0001		
Any organ failure during index hospitalization										<0.0001
No	108,553	2,950,183	3.68	19,810	287,247	6.90	1.32 (1.29, 1.34)	<0.0001		
Yes	58,940	751,841	7.84	200,618	1,407,280	14.26	1.07 (0.99, 1.16)	0.0810		
AKI during index hospitalization										<0.0001
No	141,152	3,417,975	4.13	118,658	1,012,190	11.72	1.73 (1.71, 1.75)	<0.0001		
Yes	26,341	283,549	9.29	101,770	682,337	14.91	1.17 (1.04, 1.32)	0.0107		
Shock during index hospitalization										<0.0001
No	166,144	3,686,045	4.51	203,020	1,588,099	12.78	1.75 (1.74, 1.77)	<0.0001		
Yes	1,349	15,478	8.72	17,408	106,428	16.36	1.25 (0.96, 1.62)	0.0951		
Prior hospitalization within 6 months										<0.0001
No	141,241	3,327,474	4.24	142,197	1,292,286	11.00	1.71 (1.69, 1.73)	<0.0001		
Yes	26,252	374,049	7.02	78,231	402,241	19.45	1.96 (1.91, 2.01)	<0.0001		

Table S11: Risk of all-cause hospitalization associated with sepsis (all definitions) across subgroups, using death as a competing risk. P values for interaction are unadjusted.

	No Sepsis (ref)			Sepsis			Hazard Ratio (95% CI)	P Value	P Value for interaction
	No. with Events	Person Years	Event Rate per 100	No. with Events	Person Years	Event Rate per 100			
Age group									<0.0001
All <65 years	283,275	1,498,742	18.90	149,842	366,018	40.94	1.41 (1.39, 1.42)	<0.0001	
65+ years	321,576	990,179	32.48	331,421	535,967	61.84	1.38 (1.37, 1.40)	<0.0001	
50-64 years	186,450	910,128	20.49	114,415	263,050	43.50	1.40 (1.38, 1.42)	<0.0001	
<50 years	96,825	588,614	16.45	35,427	102,968	34.41	1.43 (1.40, 1.46)	<0.0001	
Sex									0.0633
Male	275,890	1,110,995	24.83	220,045	408,805	53.83	1.40 (1.38, 1.41)	<0.0001	
Female	328,961	1,377,925	23.87	261,218	493,180	52.97	1.36 (1.35, 1.37)	<0.0001	
Race/Ethnicity									<0.0001
Asian	10,714	55,156	19.42	8,425	18,533	45.46	1.39 (1.32, 1.47)	<0.0001	
Black	77,968	279,093	27.94	70,695	112,682	62.74	1.39 (1.36, 1.42)	<0.0001	
Hispanic	40,992	180,242	22.74	32,394	63,544	50.98	1.36 (1.32, 1.39)	<0.0001	
White	383,756	1,512,054	25.38	315,346	584,355	53.96	1.37 (1.36, 1.38)	<0.0001	
All non-white	221,095	976,867	22.63	165,917	317,631	52.24	1.39 (1.37, 1.41)	<0.0001	
Health plan									<0.0001
Commercial	266,937	1,476,499	18.08	125,152	343,381	36.45	1.40 (1.38, 1.41)	<0.0001	
Medicare Advantage	337,914	1,012,422	33.38	356,111	558,604	63.75	1.37 (1.36, 1.38)	<0.0001	
Pharmacy coverage									<0.0001
No	181,967	872,619	20.85	115,058	256,588	44.84	1.39 (1.37, 1.41)	<0.0001	
Yes	422,884	1,616,302	26.16	366,205	645,397	56.74	1.37 (1.36, 1.38)	<0.0001	
Prior CVD									0.9397
No	290,899	1,529,893	19.01	157,655	436,839	36.09	1.36 (1.35, 1.37)	<0.0001	
Yes	313,952	959,028	32.74	323,608	465,147	69.57	1.39 (1.37, 1.40)	<0.0001	
# of CVD risk factors									<0.0001
<3	285,977	1,448,908	19.74	152,889	384,889	39.72	1.34 (1.33, 1.36)	<0.0001	
3+	318,874	1,040,012	30.66	328,374	517,096	63.50	1.41 (1.39, 1.42)	<0.0001	
ICU during index hospitalization									<0.0001
No	415,107	1,740,894	23.84	265,585	529,558	50.15	1.36 (1.35, 1.37)	<0.0001	
Yes	189,744	748,027	25.37	215,678	372,427	57.91	1.36 (1.35, 1.38)	<0.0001	

CVD diagnosis during index hospitalization								<0.0001	
No	304,717	1,471,436	20.71	191,886	463,331	41.41	1.38 (1.36, 1.39)	<0.0001	
Yes	300,134	1,017,485	29.50	289,377	438,654	65.97	1.35 (1.34, 1.37)	<0.0001	
Any organ failure during index hospitalization								<0.0001	
No	453,049	1,993,195	22.73	63,461	170,660	37.19	1.32 (1.31, 1.33)	<0.0001	
Yes	151,802	495,726	30.62	417,802	731,326	57.13	1.41 (1.35, 1.48)	<0.0001	
AKI during index hospitalization								<0.0001	
No	540,494	2,304,326	23.46	271,301	554,121	48.96	1.44 (1.43, 1.45)	<0.0001	
Yes	64,357	184,595	34.86	209,962	347,864	60.36	1.43 (1.32, 1.54)	<0.0001	
Shock during index hospitalization								0.2293	
No	601,916	2,478,483	24.29	449,627	845,574	53.17	1.48 (1.47, 1.49)	<0.0001	
Yes	2,935	10,437	28.12	31,636	56,411	56.08	1.46 (1.21, 1.75)	<0.0001	
Prior hospitalization within 6 months								<0.0001	
No	519,636	2,276,338	22.83	323,812	738,119	43.87	1.44 (1.43, 1.45)	<0.0001	
Yes	85,215	212,583	40.09	157,451	163,867	96.08	1.61 (1.59, 1.63)	<0.0001	

Table S12: Risk of cardiovascular hospitalization associated with sepsis (all definitions) across subgroups, using death as a competing risk. P values for interaction are unadjusted.

	No Sepsis (ref)			Sepsis			Hazard Ratio (95% CI)	P Value	P Value for interaction
	No. with Events	Person Years	Event Rate per 100	No. with Events	Person Years	Event Rate per 100			
Age group									<0.0001
All <65 years	81,181	1,968,649	4.12	61,582	547,440	11.25	1.57 (1.54, 1.61)	<0.0001	
65+ years	180,064	1,281,510	14.05	206,247	767,302	26.88	1.42 (1.40, 1.44)	<0.0001	
50-64 years	63,060	1,186,143	5.32	50,842	391,200	13.00	1.60 (1.56, 1.64)	<0.0001	
<50 years	18,121	782,506	2.32	10,740	156,240	6.87	1.61 (1.53, 1.68)	<0.0001	
Sex									<0.0001
Male	133,482	1,411,355	9.46	126,422	581,976	21.72	1.42 (1.40, 1.44)	<0.0001	
Female	127,763	1,838,805	6.95	141,407	732,766	19.30	1.43 (1.41, 1.46)	<0.0001	
Race/Ethnicity									0.0006
Asian	4,567	68,998	6.62	4,618	25,830	17.88	1.34 (1.23, 1.47)	<0.0001	
Black	37,084	365,637	10.14	42,385	166,599	25.44	1.42 (1.38, 1.46)	<0.0001	
Hispanic	16,939	232,796	7.28	17,799	90,771	19.61	1.33 (1.28, 1.39)	<0.0001	
White	171,886	1,986,376	8.65	177,931	856,362	20.78	1.43 (1.41, 1.45)	<0.0001	
All non-white	89,359	1,263,784	7.07	89,898	458,381	19.61	1.43 (1.40, 1.45)	<0.0001	
Health plan									<0.0001
Commercial	76,461	1,908,542	4.01	48,447	492,057	9.85	1.55 (1.52, 1.59)	<0.0001	
Medicare Advantage	184,784	1,341,618	13.77	219,382	822,685	26.67	1.39 (1.37, 1.41)	<0.0001	
Pharmacy coverage									<0.0001
No	70,172	1,139,965	6.16	58,798	370,641	15.86	1.44 (1.41, 1.48)	<0.0001	
Yes	191,073	2,110,194	9.05	209,031	944,101	22.14	1.42 (1.40, 1.44)	<0.0001	
Prior CVD									<0.0001
No	78,951	2,010,555	3.93	57,480	637,568	9.02	1.48 (1.45, 1.51)	<0.0001	
Yes	182,294	1,239,605	14.71	210,349	677,175	31.06	1.41 (1.39, 1.43)	<0.0001	
# of CVD risk factors									<0.0001
<3	101,518	1,875,800	5.41	69,903	549,927	12.71	1.41 (1.39, 1.44)	<0.0001	
3+	159,727	1,374,360	11.62	197,926	764,815	25.88	1.44 (1.42, 1.46)	<0.0001	
ICU during index hospitalization									<0.0001
No	155,273	2,324,377	6.68	137,926	779,891	17.69	1.43 (1.41, 1.45)	<0.0001	
Yes	105,972	925,783	11.45	129,903	534,851	24.29	1.39 (1.36, 1.42)	<0.0001	

CVD diagnosis during index hospitalization								<0.0001	
No	66,913	2,010,432	3.33	67,654	709,162	9.54	1.51 (1.48, 1.54)	<0.0001	
Yes	194,332	1,239,728	15.68	200,175	605,580	33.06	1.38 (1.36, 1.40)	<0.0001	
Any organ failure during index hospitalization								<0.0001	
No	181,765	2,617,466	6.94	27,878	243,137	11.47	1.35 (1.33, 1.37)	<0.0001	
Yes	79,480	632,694	12.56	239,951	1,071,605	22.39	1.52 (1.43, 1.62)	<0.0001	
AKI during index hospitalization								<0.0001	
No	224,763	3,016,407	7.45	140,743	806,814	17.44	1.50 (1.48, 1.51)	<0.0001	
Yes	36,482	233,753	15.61	127,086	507,928	25.02	1.52 (1.38, 1.67)	<0.0001	
Shock during index hospitalization								<0.0001	
No	259,601	3,237,222	8.02	250,427	1,231,974	20.33	1.59 (1.57, 1.60)	<0.0001	
Yes	1,644	12,938	12.71	17,402	82,768	21.03	1.34 (1.02, 1.76)	0.0366	
Prior hospitalization within 6 months								<0.0001	
No	223,079	2,939,026	7.59	175,757	1,035,258	16.98	1.54 (1.52, 1.55)	<0.0001	
Yes	38,166	311,134	12.27	92,072	279,484	32.94	1.73 (1.70, 1.77)	<0.0001	

Table S13: Risk of the composite of all-cause death and all-cause hospitalization associated with sepsis (all definitions) across subgroups. P values for interaction are unadjusted.

	No Sepsis (ref)			Sepsis			Hazard Ratio (95% CI)	P Value	P Value for interaction
	No. with Events	Person Years	Event Rate per 100	No. with Events	Person Years	Event Rate per 100			
Age group									<0.0001
All <65 years	291,368	1,498,742	19.44	157,129	366,018	42.93	1.41 (1.39, 1.43)	<0.0001	
65+ years	370,101	990,179	37.38	381,099	535,967	71.10	1.31 (1.30, 1.32)	<0.0001	
50-64 years	193,140	910,128	21.22	120,553	263,050	45.83	1.41 (1.39, 1.43)	<0.0001	
<50 years	98,228	588,614	16.69	36,576	102,968	35.52	1.43 (1.40, 1.46)	<0.0001	
Sex									<0.0001
Male	302,445	1,110,995	27.22	245,964	408,805	60.17	1.36 (1.35, 1.38)	<0.0001	
Female	359,024	1,377,925	26.06	292,264	493,180	59.26	1.33 (1.32, 1.34)	<0.0001	
Race/Ethnicity									<0.0001
Asian	11,681	55,156	21.18	9,447	18,533	50.97	1.37 (1.30, 1.44)	<0.0001	
Black	84,494	279,093	30.27	78,071	112,682	69.28	1.36 (1.34, 1.39)	<0.0001	
Hispanic	43,504	180,242	24.14	35,161	63,544	55.33	1.34 (1.31, 1.38)	<0.0001	
White	425,411	1,512,053	28.13	356,315	584,355	60.98	1.33 (1.32, 1.34)	<0.0001	
All non-white	236,058	976,867	24.16	181,913	317,631	57.27	1.38 (1.36, 1.39)	<0.0001	
Health plan									<0.0001
Commercial	274,975	1,476,499	18.62	131,862	343,381	38.40	1.40 (1.39, 1.42)	<0.0001	
Medicare Advantage	386,464	1,012,422	38.17	406,366	558,604	72.75	1.31 (1.30, 1.33)	<0.0001	
Pharmacy coverage									0.0021
No	197,504	872,619	22.63	128,428	256,588	50.05	1.36 (1.34, 1.37)	<0.0001	
Yes	463,965	1,616,302	28.71	409,800	645,397	63.50	1.34 (1.33, 1.35)	<0.0001	
Prior CVD									0.0684
No	311,293	1,529,893	20.35	172,568	436,839	39.50	1.34 (1.33, 1.35)	<0.0001	
Yes	350,176	959,028	36.51	365,660	465,147	78.61	1.34 (1.33, 1.36)	<0.0001	
# of CVD risk factors									<0.0001
<3	313,403	1,448,908	21.63	174,566	384,889	45.35	1.32 (1.30, 1.33)	<0.0001	
3+	348,066	1,040,012	33.47	363,662	517,096	70.33	1.38 (1.36, 1.39)	<0.0001	
ICU during index hospitalization									<0.0001
No	453,740	1,740,894	26.06	295,253	529,558	55.75	1.33 (1.31, 1.34)	<0.0001	
Yes	207,729	748,027	27.77	242,975	372,427	65.24	1.33 (1.32, 1.35)	<0.0001	

CVD diagnosis during index hospitalization								<0.0001	
No	327,156	1,471,436	22.23	210,233	463,330	45.37	1.36 (1.35, 1.37)	<0.0001	
Yes	334,313	1,017,485	32.86	327,995	438,654	74.77	1.30 (1.29, 1.31)	<0.0001	
Any organ failure during index hospitalization								<0.0001	
No	488,007	1,993,195	24.48	67,929	170,660	39.80	1.30 (1.29, 1.31)	<0.0001	
Yes	173,462	495,726	34.99	470,299	731,326	64.31	1.29 (1.23, 1.35)	<0.0001	
AKI during index hospitalization								<0.0001	
No	587,731	2,304,326	25.51	302,186	554,121	54.53	1.49 (1.48, 1.50)	<0.0001	
Yes	73,738	184,595	39.95	236,042	347,864	67.85	1.33 (1.23, 1.43)	<0.0001	
Shock during index hospitalization								<0.0001	
No	657,871	2,478,483	26.54	500,061	845,574	59.14	1.52 (1.51, 1.53)	<0.0001	
Yes	3,598	10,437	34.47	38,167	56,411	67.66	1.35 (1.14, 1.59)	0.0004	
Prior hospitalization within 6 months								<0.0001	
No	567,958	2,276,337	24.95	361,651	738,119	49.00	1.48 (1.47, 1.49)	<0.0001	
Yes	93,511	212,583	43.99	176,577	163,867	107.76	1.71 (1.69, 1.74)	<0.0001	

Table S14: Risk of the composite of all-cause death and cardiovascular hospitalization associated with sepsis (all definitions) across subgroups. P values for interaction are unadjusted.

	No Sepsis (ref)			Sepsis			Hazard Ratio (95% CI)	P Value	P Value for interaction
	No. with Events	Person Years	Event Rate per 100	No. with Events	Person Years	Event Rate per 100			
Age group									<0.0001
All <65 years	98,844	1,968,649	5.02	78,840	547,440	14.40	1.61 (1.58, 1.65)	<0.0001	
65+ years	261,559	1,281,510	20.41	298,674	767,302	38.93	1.30 (1.29, 1.32)	<0.0001	
50-64 years	77,651	1,186,143	6.55	65,311	391,200	16.70	1.65 (1.62, 1.69)	<0.0001	
<50 years	21,193	782,506	2.71	13,529	156,240	8.66	1.65 (1.58, 1.72)	<0.0001	
Sex									<0.0001
Male	179,941	1,411,355	12.75	177,166	581,976	30.44	1.38 (1.36, 1.40)	<0.0001	
Female	180,462	1,838,805	9.81	200,348	732,766	27.34	1.36 (1.34, 1.37)	<0.0001	
Race/Ethnicity									<0.0001
Asian	6,266	68,998	9.08	6,615	25,831	25.61	1.34 (1.24, 1.44)	<0.0001	
Black	48,976	365,637	13.39	57,135	166,599	34.29	1.37 (1.34, 1.41)	<0.0001	
Hispanic	21,603	232,796	9.28	23,398	90,771	25.78	1.33 (1.28, 1.38)	<0.0001	
White	243,636	1,986,376	12.27	255,958	856,362	29.89	1.35 (1.33, 1.36)	<0.0001	
All non-white	116,767	1,263,784	9.24	121,556	458,381	26.52	1.41 (1.39, 1.43)	<0.0001	
Health plan									<0.0001
Commercial	92,971	1,908,542	4.87	62,512	492,057	12.70	1.60 (1.57, 1.63)	<0.0001	
Medicare Advantage	267,432	1,341,618	19.93	315,002	822,685	38.29	1.30 (1.29, 1.32)	<0.0001	
Pharmacy coverage									0.2842
No	97,088	1,139,965	8.52	84,099	370,641	22.69	1.38 (1.35, 1.40)	<0.0001	
Yes	263,315	2,110,194	12.48	293,415	944,101	31.08	1.36 (1.35, 1.38)	<0.0001	
Prior CVD									<0.0001
No	119,463	2,010,555	5.94	91,352	637,568	14.33	1.42 (1.40, 1.45)	<0.0001	
Yes	240,940	1,239,605	19.44	286,162	677,175	42.26	1.33 (1.32, 1.35)	<0.0001	
# of CVD risk factors									<0.0001
<3	149,962	1,875,800	7.99	111,142	549,927	20.21	1.34 (1.32, 1.36)	<0.0001	
3+	210,441	1,374,360	15.31	266,372	764,815	34.83	1.39 (1.37, 1.41)	<0.0001	
ICU during index hospitalization									<0.0001
No	225,733	2,324,377	9.71	199,256	779,891	25.55	1.35 (1.34, 1.37)	<0.0001	
Yes	134,670	925,783	14.55	178,258	534,851	33.33	1.33 (1.31, 1.35)	<0.0001	

CVD diagnosis during index hospitalization								<0.0001	
No	113,795	2,010,432	5.66	112,143	709,162	15.81	1.46 (1.43, 1.48)	<0.0001	
Yes	246,608	1,239,728	19.89	265,371	605,580	43.82	1.29 (1.28, 1.31)	<0.0001	
Any organ failure during index hospitalization								0.0003	
No	246,419	2,617,466	9.41	38,381	243,137	15.79	1.32 (1.31, 1.34)	<0.0001	
Yes	113,984	632,694	18.02	339,133	1,071,605	31.65	1.28 (1.21, 1.35)	<0.0001	
AKI during index hospitalization								<0.0001	
No	309,359	3,016,407	10.26	203,143	806,814	25.18	1.61 (1.60, 1.62)	<0.0001	
Yes	51,044	233,753	21.84	174,371	507,928	34.33	1.35 (1.23, 1.47)	<0.0001	
Shock during index hospitalization								0.0107	
No	357,892	3,237,222	11.06	349,974	1,231,974	28.41	1.67 (1.66, 1.69)	<0.0001	
Yes	2,511	12,938	19.41	27,540	82,768	33.27	1.27 (1.04, 1.56)	0.0220	
Prior hospitalization within 6 months								<0.0001	
No	357,916	3,237,374	11.06	359,351	1,258,655	28.55	1.67 (1.66, 1.69)	<0.0001	
Yes	2,487	12,786	19.45	18,163	56,087	32.38	1.32 (1.06, 1.64)	0.0129	

Table S15. Risk of each of the outcomes of interest associated with sepsis (all definitions) across subgroups defined by the presence of any infection and by the most common infection subtypes. P values for interaction are unadjusted.

	No Sepsis (ref)			Sepsis			Hazard Ratio (95% CI)	P Value	P Value for interaction
	No. with Events	Person Years	Event Rate per 100	No. with Events	Person Years	Event Rate per 100			
Infection during index hospitalization									
No infection	N=1,114,981			N=7,174					
Mortality	130,463	2,818,188	4.63	1,457	21,570	6.75	1.12 (1.06, 1.17)	<0.0001	<0.0001
All-cause hospitalization	466,191	1,894,523	24.61	4,194	11,541	36.34	1.39 (1.34, 1.43)	<0.0001	<0.0001
CVD hospitalization	210,481	2,451,875	8.58	2,559	16,111	15.88	1.68 (1.61, 1.75)	<0.0001	<0.0001
Death or all-cause hospitalization	510,098	1,894,523	26.92	4,467	11,541	38.71	1.30 (1.26, 1.34)	<0.0001	<0.0001
Death or CVD hospitalization	286,597	2,451,875	11.69	3,121	16,111	19.37	1.42 (1.37, 1.47)	<0.0001	<0.0001
Any infection	N=334,840			N=801,499					
Mortality	37,030	883,335	4.19	218,971	1,672,957	13.09	1.35 (1.33, 1.37)	<0.0001	<0.0001
All-cause hospitalization	138,660	594,397	23.33	477,069	890,445	53.58	1.34 (1.33, 1.35)	<0.0001	0.0251
CVD hospitalization	50,764	798,285	6.36	265,270	1,298,631	20.43	1.38 (1.36, 1.40)	<0.0001	0.0488
Death or all-cause hospitalization	151,371	594,397	25.47	533,761	890,445	59.94	1.31 (1.30, 1.33)	<0.0001	0.0018
Death or CVD hospitalization	73,806	798,285	9.25	374,393	1,298,631	28.83	1.35 (1.34, 1.37)	<0.0001	0.3253
Pulmonary	N=61,653			N=177,274					
Mortality	9,919	138,737	7.15	55,118	352,335	15.64	1.17 (1.07, 1.27)	0.0004	
All-cause hospitalization	26,671	94,698	28.16	111,620	178,787	62.43	1.39 (1.33, 1.46)	<0.0001	
CVD hospitalization	12,752	120,380	10.59	70,233	255,750	27.46	1.38 (1.29, 1.48)	<0.0001	
Death or all-cause hospitalization	29,933	94,698	31.61	124,444	178,787	69.60	1.31 (1.25, 1.38)	<0.0001	
Death or CVD hospitalization	18,651	120,380	15.49	94,685	255,750	37.02	1.26 (1.19, 1.34)	<0.0001	
Bacterial/fungal/iatrogenic/sepsis/bacteremia	N=44,498			N=175,142					
Mortality	4,109	120,625	3.41	42,583	370,595	11.49	1.68 (1.62, 1.75)	<0.0001	
All-cause hospitalization	17,606	82,880	21.24	100,380	202,990	49.45	1.46 (1.43, 1.49)	<0.0001	
CVD hospitalization	5,745	110,198	5.21	50,083	298,827	16.76	1.54 (1.49, 1.59)	<0.0001	
Death or all-cause hospitalization	19,002	82,880	22.93	112,058	202,990	55.20	1.46 (1.43, 1.49)	<0.0001	
Death or CVD hospitalization	8,450	110,198	7.67	73,041	298,827	24.44	1.58 (1.54, 1.63)	<0.0001	
Genitourinary	N=53,178			N=109,157					
Mortality	8,981	133,353	6.73	35,788	223,271	16.03	1.11 (1.03, 1.20)	0.0088	
All-cause hospitalization	23,478	86,849	27.03	68,371	112,441	60.81	1.34 (1.28, 1.41)	<0.0001	
CVD hospitalization	9,410	117,945	7.98	40,115	166,706	24.06	1.44 (1.34, 1.54)	<0.0001	

Sepsis and cardiovascular events

Death or all-cause hospitalization	27,046	86,849	31.14	78,044	112,441	69.41	1.25 (1.20, 1.31)	<0.0001
Death or CVD hospitalization	15,333	117,945	13.00	58,145	166,706	34.88	1.23 (1.17, 1.31)	<0.0001
Multiple		N=59,250			N=267,444			
Mortality	6,789	159,187	4.26	69,181	559,739	12.36	1.26 (1.22, 1.30)	<0.0001
All-cause hospitalization	24,138	108,199	22.31	152,437	309,456	49.26	1.36 (1.34, 1.39)	<0.0001
CVD hospitalization	8,374	145,144	5.77	79,814	448,743	17.79	1.49 (1.45, 1.53)	<0.0001
Death or all-cause hospitalization	26,628	108,199	24.61	171,785	309,456	55.51	1.32 (1.30, 1.34)	<0.0001
Death or CVD hospitalization	12,816	145,144	8.83	116,752	448,743	26.02	1.37 (1.34, 1.41)	<0.0001
Other		N=116,261			N=72,482			
Mortality	7,232	331,433	2.18	16,301	167,017	9.76	1.40 (1.27, 1.54)	<0.0001
All-cause hospitalization	46,767	221,772	21.09	44,261	86,771	51.01	1.30 (1.24, 1.35)	<0.0001
CVD hospitalization	14,483	304,618	4.75	25,025	128,604	19.46	1.48 (1.39, 1.58)	<0.0001
Death or all-cause hospitalization	48,762	221,772	21.99	47,430	86,771	54.66	1.29 (1.24, 1.35)	<0.0001
Death or CVD hospitalization	18,556	304,618	6.09	31,770	128,604	24.70	1.45 (1.37, 1.54)	<0.0001

Figure S1. Flow chart demonstrating study inclusion/exclusion criteria and sepsis groups. *Abbreviations: CVD, cardiovascular disease; DRG, Disease-Related Group; LOS, length of stay; OLDW, OptumLabs® Data Warehouse*

