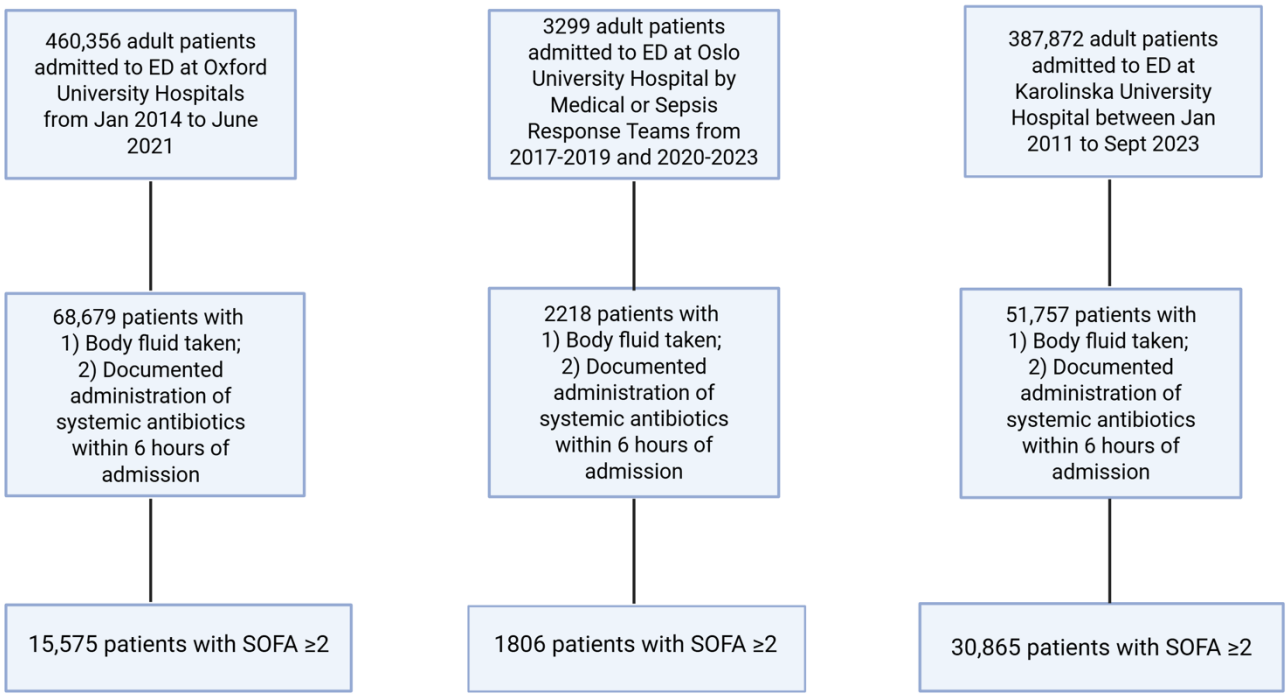
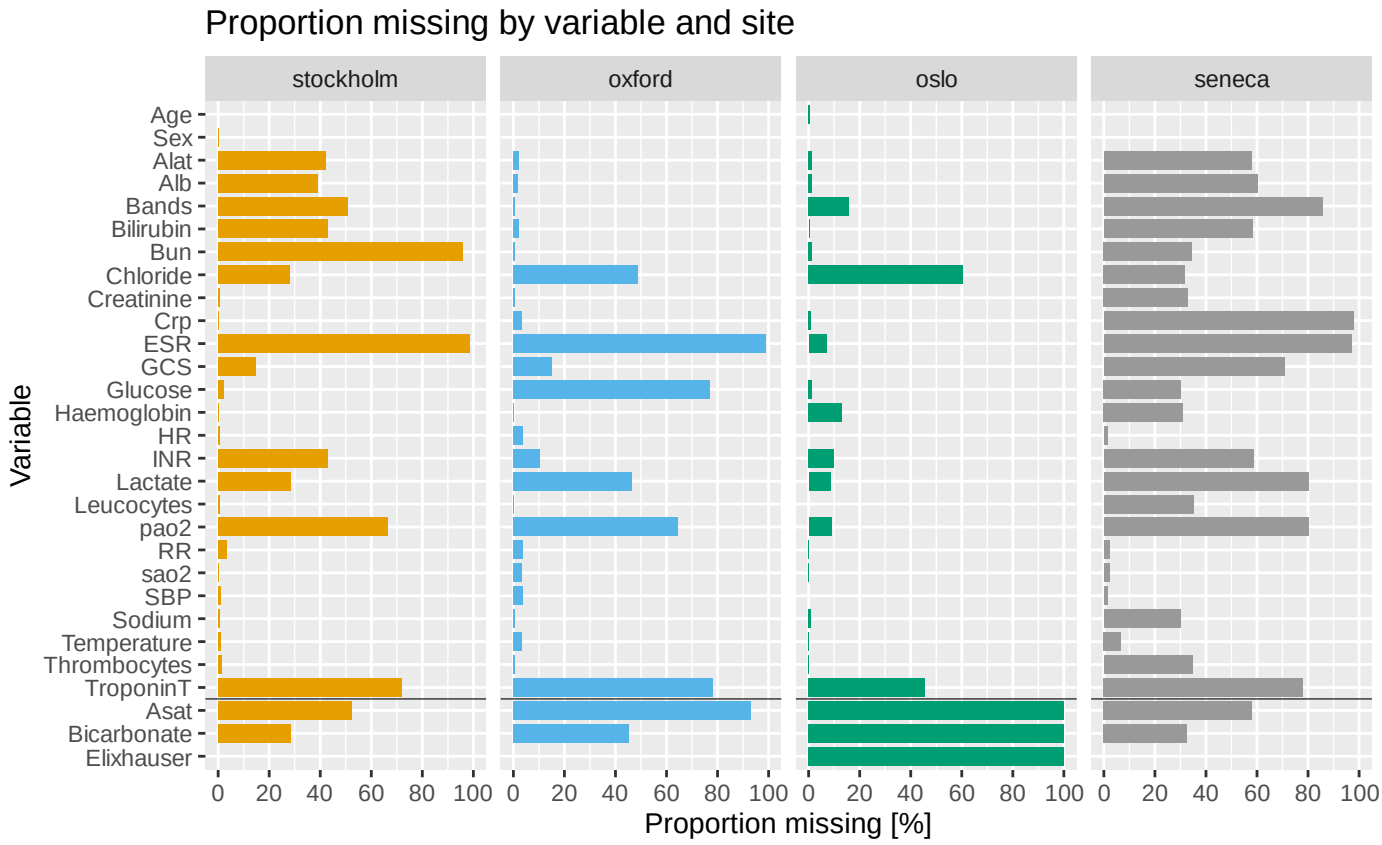
Supplementary Data

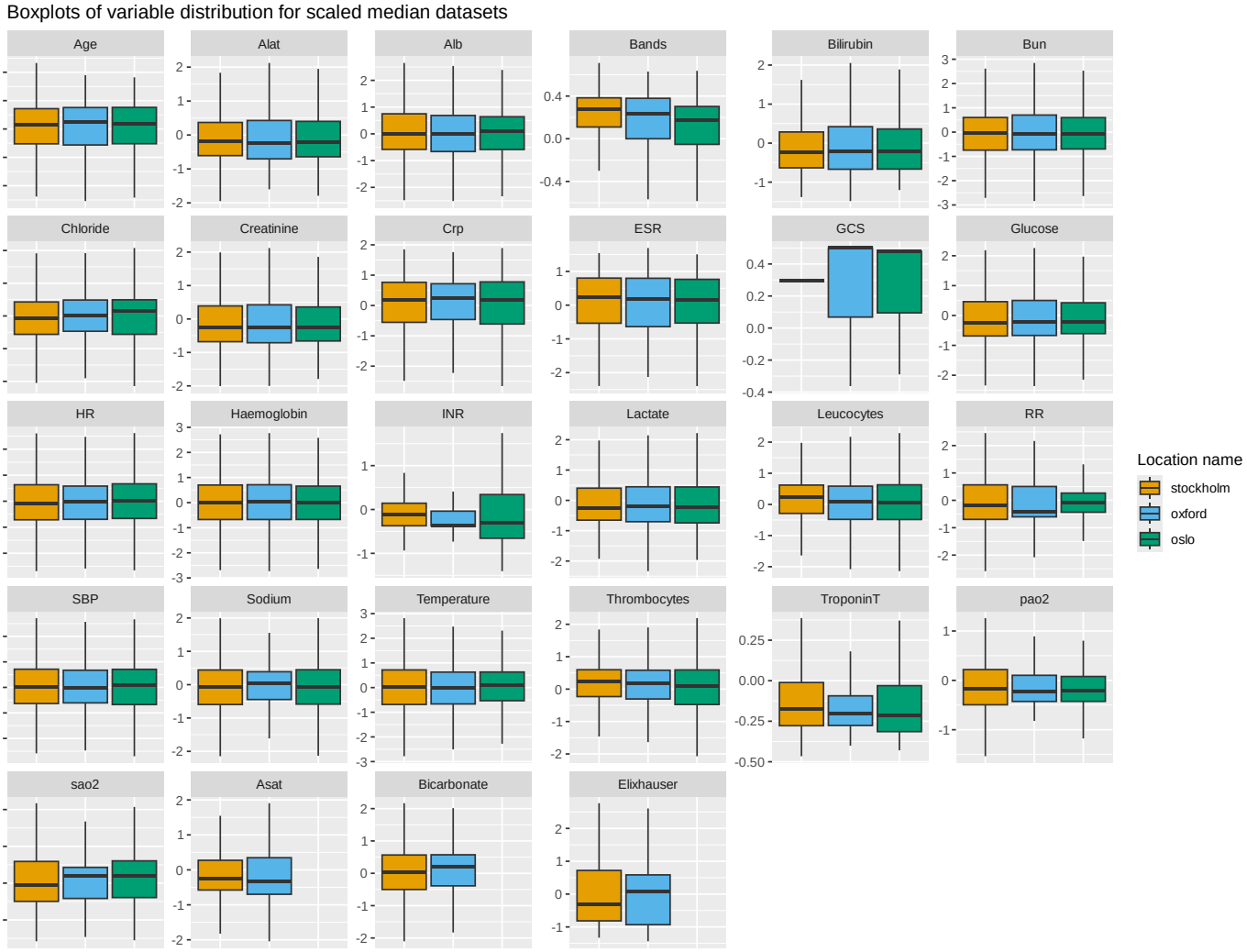
eSupplementary Figure 1 Flowchart of patient selection in the Oxford, Oslo and Stockholm cohorts (left: Oxford, middle: Oslo, right: Stockholm). Body fluid: blood, urine and/or cerebrospinal fluid. ED: Emergency Department, SOFA: Sequential Organ Failure Assessment.



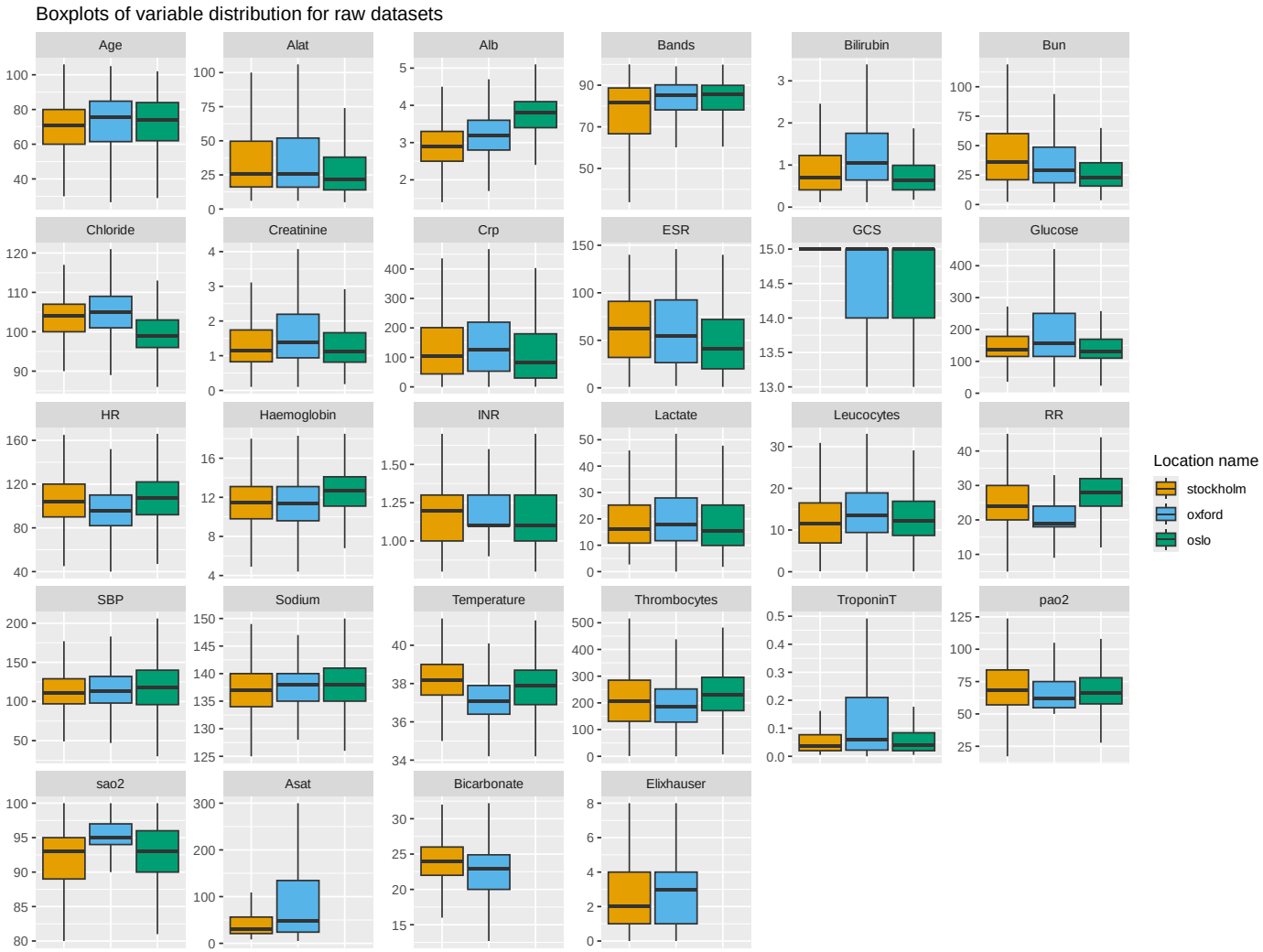
eSupplementary Figure 2 Proportions of missingness by variable in the Oslo, Oxford and Stockholm cohorts. Seneca derivation dataset missingness included in grey as a reference, numerical data extracted from Seymour et al [1]. Neutrophil granulocytes and urea were used instead of bands and blood urea nitrogen, respectively, in Oxford, Stockholm and Oslo. HR: Heart Rate, SBP: Systolic Blood Pressure, PaO2: partial pressure of oxygen, RR: Respiratory Rate, SaO2: oxygen saturation, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, CRP: C-Reactive Protein, ESR: Estimated Sedimentation Rate, ALAT: Alanine Transaminases, ASAT: Aspartate Transaminases, BUN: Blood Urea Nitrogen



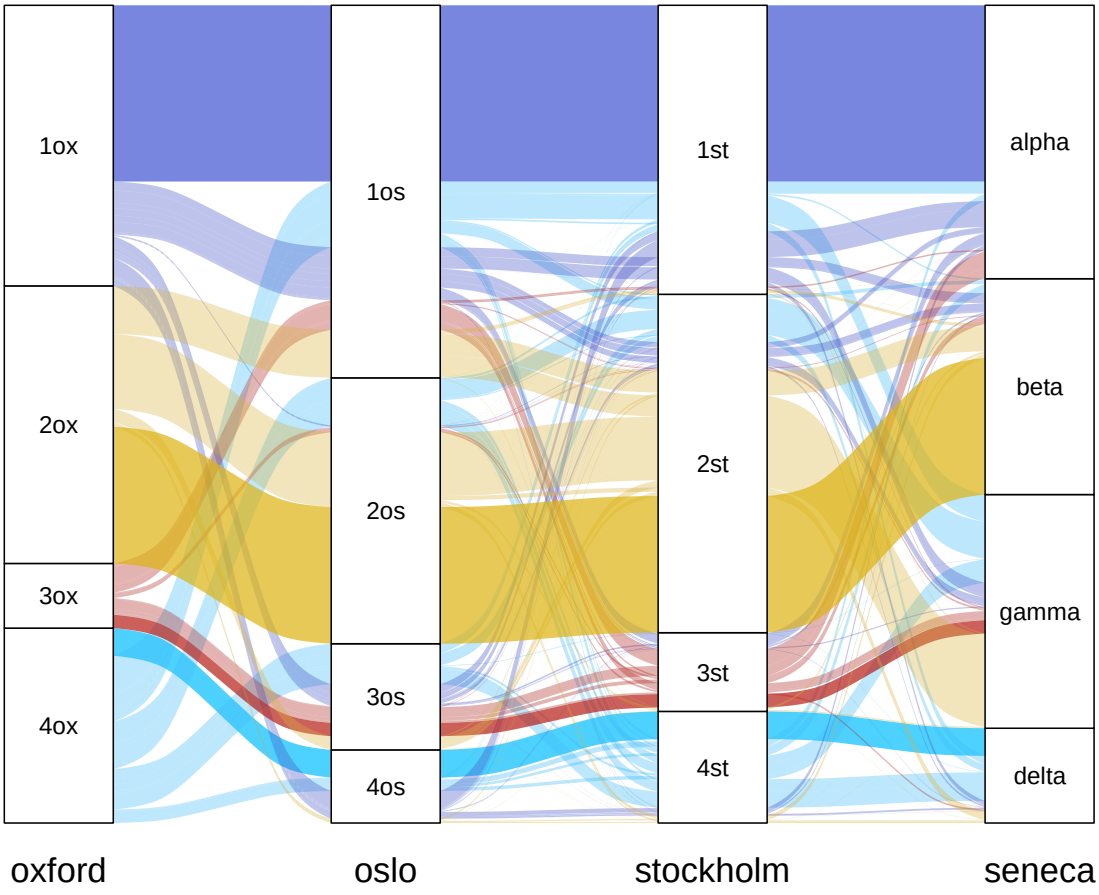
eSupplementary Figure 3 Boxplots of scaled medians and IQR by variable and cohort. Neutrophil granulocytes and urea were used instead of bands and blood urea nitrogen, respectively, in Oxford, Stockholm and Oslo. HR: Heart Rate, SBP: Systolic Blood Pressure, PaO2: partial pressure of oxygen, RR: Respiratory Rate, SaO2: oxygen saturation, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, CRP: C-Reactive Protein, ESR: Estimated Sedimentation Rate, ALAT: Alanine Transaminases, ASAT: Aspartate Transaminases, BUN: Blood Urea Nitrogen



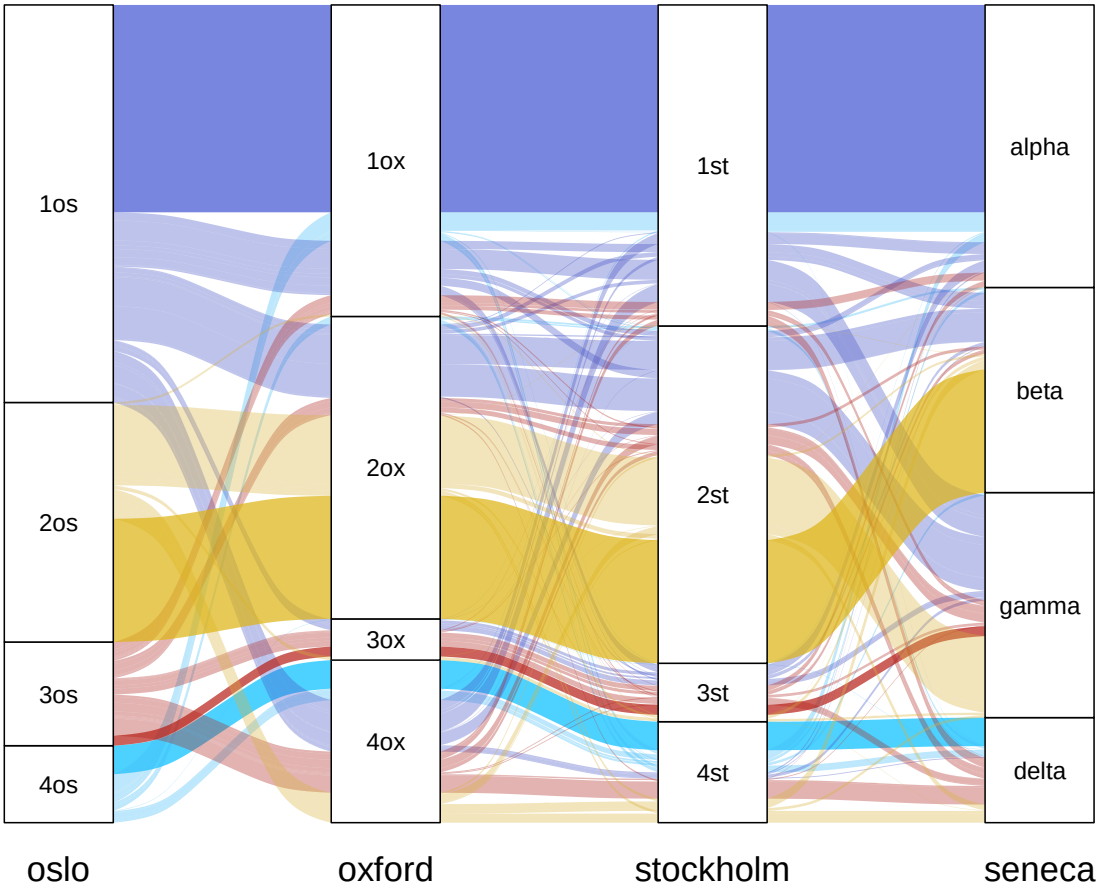
eSupplementary Figure 4 Boxplots of raw medians and IQR by variable and cohort. Neutrophil granulocytes and urea were used instead of bands and blood urea nitrogen, respectively, in Oxford, Stockholm and Oslo. HR: Heart Rate, SBP: Systolic Blood Pressure, PaO2: partial pressure of oxygen, RR: Respiratory Rate, SaO2: oxygen saturation, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, CRP: C-Reactive Protein, ESR: Estimated Sedimentation Rate, ALAT: Alanine Transaminases, ASAT: Aspartate Transaminases, BUN: Blood Urea Nitrogen



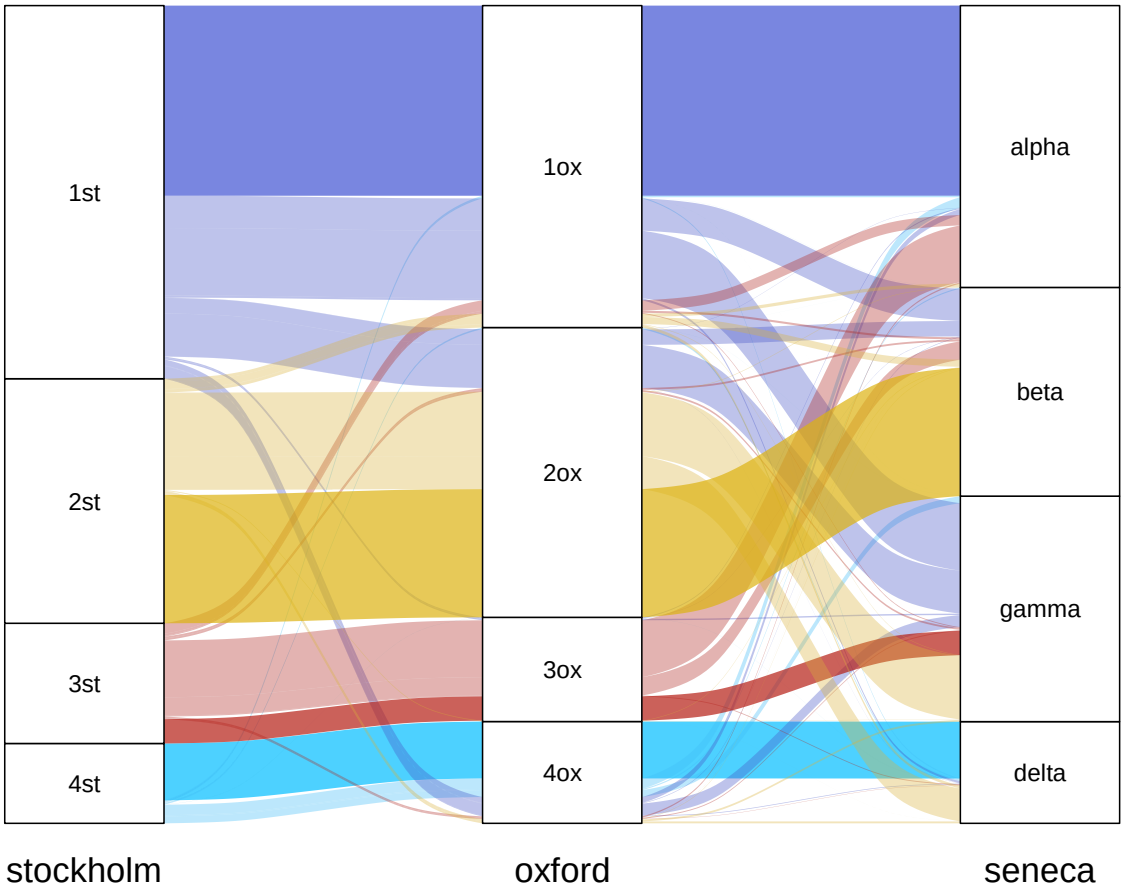
eSupplementary Figure 5 Alluvial plot showing differences in patients from a given site being assigned to phenotypes derived from individual sites incl. SENECA. In this example, patients are from the Oxford dataset with the common set of 26 variables. Left-most column is assigned with the centroid positions from the Oxford clustering results (i.e., calculated using the same dataset); meanwhile, 'oslo' indicates the assignment of Oxford patients to the centroids derived from the Oslo dataset based on the shortest Euclidean distance for each Oxford patient; similarly for 'stockholm' and 'seneca' with their respective site-derived centroids. Coloured according to Oxford phenotypes with phenotype ordering as close as possible to SENECA. Fleiss kappa for agreement is 0.49, and the percentage agreement between all is 43%. The Adjusted Rand Indices compared to Oxford are 0.32 Oslo, 0.54 Stockholm, and to 0.37 SENECA.



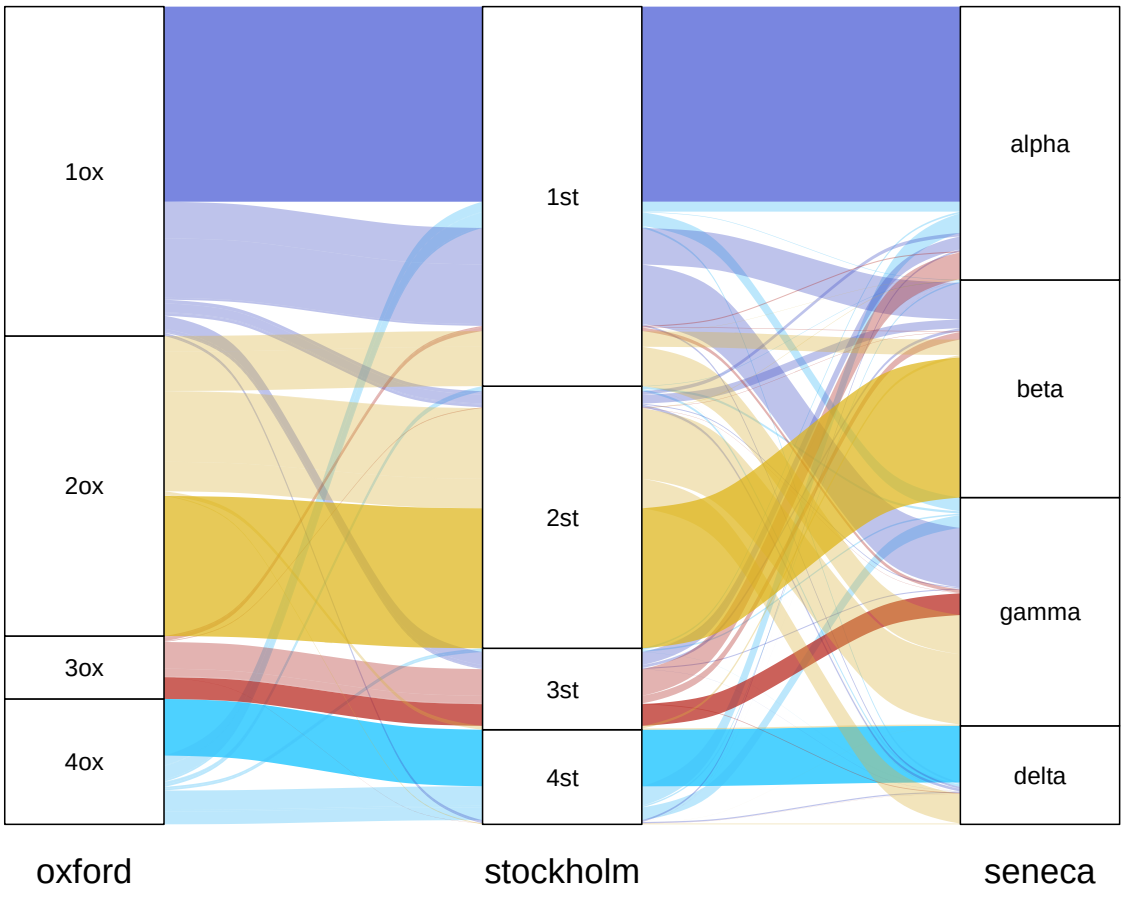
eSupplementary Figure 6 Alluvial plot showing differences in patients from a given site being assigned to phenotypes derived from individual sites incl. SENECA. In this example, patients are from the Oslo dataset with the common set of 26 variables. Left-most column is assigned with the centroid positions from the Oslo clustering result (i.e. calculated using the same dataset); meanwhile, 'oxford' indicates the assignment of Oslo patients to the centroids derived from the Oxford dataset based on the shortest Euclidean distance for each Oslo patient; similarly for 'stockholm' and 'seneca' with their respective site-derived centroids. Coloured according to Oslo phenotypes with phenotype ordering as close as possible to SENECA. Fleiss kappa for agreement is 0.50, and the percentage agreement between all is 45%. The Adjusted Rand Indices compared to Oxford are 0.33 Oslo, 0.37 Stockholm, and 0.27 SENECA.



eSupplementary Figure 7 Alluvial plot showing differences in patients from a given site being assigned to phenotypes derived from individual sites incl. SENECA using all 29 variables. In this example, patients are from the Stockholm dataset. Left-most column is assigned with the centroid positions from the Stockholm clustering result (i.e. calculated using the same dataset), while the others are by assigning clusters using centroid information from the respective sites based on the shortest Euclidean distance for each Stockholm patient. Coloured according to Stockholm phenotypes with phenotype ordering as close as possible to SENECA. Fleiss kappa for agreement is 0.48, and the percentage agreement between all is 49%. The adjusted rand index is comparing Stockholm to Oxford 0.60, and to SENECA 0.25.



eSupplementary Figure 8 Alluvial plot showing differences in patients from a given site being assigned to phenotypes derived from individual sites incl. SENECA using all 29 variables. In this example, patients are from the Oxford dataset. Left-most column is assigned with the centroid positions from the Oxford clustering result (i.e. calculated using the same dataset), while the others are by assigning clusters using centroid information from the respective sites based on the shortest Euclidean distance for each Oxford patient. Coloured according to Oxford phenotypes with phenotype ordering as close as possible to SENECA. Fleiss kappa for agreement is 0.49, and the percentage agreement between all is 51%. The adjusted rand index comparing Oxford to Stockholm is 0.57, and to SENECA 0.26.



eSupplementary Table 1 Variables and their units included in the analysis, as originally selected in the SENECA data analyzed by Seymour et al [1], and using the same transformations. HR: Heart Rate, SBP: Systolic Blood Pressure, PaO2: partial pressure of oxygen, RR: Respiratory Rate, SpO2: oxygen saturation, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, CRP: C-Reactive Protein, ESR: Estimated Sedimentation Rate, ALAT: Alanine Transaminases, ASAT: Aspartate Transaminases, BUN: Blood Urea Nitrogen, IU: International Units.

Variables	**Units in SENECA data used by Seymour et al.**	**Transformation**
Age	years	-
Sex	M=1, F=0	-
HR	beats/min	-
SBP	mmHg	-
RR	breaths/min	-
PaO2	mmHg	-
SpO2	% [0-100]	Ln(101-sao2)
Temperature	°C	-
GCS	-	-
Elixhauser	-	-
Haemoglobin	g/dL	-
Leucocytes	$x10^9$/L	Ln
Bands	% [0-100]	Ln
Thrombocytes	$x10^9$/L	Ln
INR	-	Ln
CRP	mg/L	Ln
ESR	mm/h	Ln
ALAT	IU/L	Ln
ASAT	IU/L	Ln
Bilirubin	mg/dL	Ln
Albumin	g/dL	-
Creatinine	mg/dL	Ln
BUN	mg/dL	Ln
Chloride	mEq/L	-
Sodium	mEq/L	-
Bicarbonate	mEq/L	-
Lactate	mmol/L	Ln
Glucose	mg/dL	Ln
Troponin T	ng/mL	Ln

eSupplementary Table 2 Variables and their units in the SENECA, Stockholm, Oslo and Oxford datasets. HR: Heart Rate, SBP: Systolic Blood Pressure, PaO2: partial pressure of oxygen, RR: Respiratory Rate, SpO2: oxygen saturation, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, CRP: C-Reactive Protein, ESR: Estimated Sedimentation Rate, ALAT: Alanine Transaminases, ASAT: Aspartate Transaminases, BUN: Blood Urea Nitrogen, IU: International Units. [a] Lactate was expressed as mmol/L for all calculations in accordance with the original methodology in Seymour et al. before being converted to mg/dL for wider clinical familiarity among readers [1].

Variables	Units in SENECA data used by Seymour et al.	Variables in Stockholm, units	Variables in Oslo, units	Variables in Oxford, units
Age	years	years	Years	years
Sex	M=1, F=0	M=1, F=0	M=1, F=0	M=1, F=0
HR	beats/min	beats/min	beats/min	beats/min
SBP	mmHg	mmHg	mmHg	mmHg
RR	breaths/min	breaths/min	breaths/min	breaths/min
paO2	mmHg	mmHg	mmHg	mmHg
SpO2	%	% [0-100]	% [0-100]	% [0-100]
Temperature	°C	°C	°C	°C
GCS	-	-	-	-
Elixhauser	-	-	*Not Available*	-
Haemoglobin	g/dL	g/dL	g/dL	g/dL
Leucocytes	$x10^9$/L	$x10^9$/L	$x10^9$/L	$x10^9$/L
Bands (SENECA) / Neutrophils (other datasets)	% of leucocytes	% neutrophils/leucocytes	% neutrophils/leucocytes	% neutrophils/leucocytes
Thrombocytes	$x10^9$/L	$x10^9$/L	$x10^9$/L	$x10^9$/L
INR	-	-	-	-
CRP	mg/L	mg/L	mg/L	mg/L
ESR	mm/h	mm/h	mm/h	mm/h
ALAT	IU/L	IU/L	IU/L	IU/L
ASAT	IU/L	IU/L	*Not Available*	IU/L
Bilirubin	mg/dL	mg/dL	mg/dL	mg/dL
Albumin	g/dL	g/dL	g/dL	g/dL

Creatinine	mg/dL	mg/dL	mg/dL	mg/dL
BUN (SENECA) / Urea (other datasets)	mg/dL	Urea mg/dL	Urea mg/dL	Urea mg/dL
Chloride	mEq/L (equivalent to mmol/L)	mmol/L	mmol/L	mmol/L
Sodium	mEq/L (equivalent to mmol/L)	mmol/L	mmol/L	mmol/L
Bicarbonate	mEq/L (equivalent to mmol/L)	mmol/L	*Not Available*	mmol/L
Lactate[a]	mmol/L	mmol/L	mmol/L	mmol/L
Glucose	mg/dL	mg/dL	mg/dL	mg/dL
Troponin T	ng/mL	ng/mL	ng/mL	ng/mL

eSupplementary Table 3 Characteristics of the four phenotypes derived from applying the same consensus clustering approach on the Oslo cohort (1os, 2os, 3os, 4os), and the characteristics of the four phenotypes when Oslo patients are assigned to the closest SENECA phenotypes in Euclidean space. Data source: Oslo, Variable set: 26v. Expressed as median [IQR], mean (SD), or no. (%).

		Phenotype							
		oslo				seneca			
Variable	Total	1os	2os	3os	4os	alpha	beta	gamma	delta
No. of patients (%)	1806 (100%)	878 (49%)	529 (29%)	229 (13%)	170 (9%)	624 (35%)	453 (25%)	497 (28%)	232 (13%)
Age, years	71 (17)	69 (18)	77 (12)	66 (17)	68 (18)	66 (19)	78 (12)	70 (16)	72 (15)
Sex, male no. (%)	1068 (59%)	478 (54%)	320 (60%)	164 (72%)	106 (62%)	351 (56%)	283 (62%)	273 (55%)	161 (69%)
ALAT, IU/L	22 [15 - 38]	20 [14 - 30]	18 [13 - 30]	49 [28 - 125]	34 [22 - 57]	22 [16 - 34]	17 [12 - 27]	21 [14 - 35]	53 [29 - 143]
Albumin, g/dL	3.7 (0.57)	4.0 (0.43)	3.4 (0.45)	3.3 (0.57)	3.9 (0.63)	4.2 (0.41)	3.6 (0.47)	3.4 (0.48)	3.4 (0.55)
Bands, %	86 [79 - 89]	85 [79 - 89]	87 [81 - 90]	87 [79 - 92]	83 [76 - 88]	84 [77 - 89]	85 [79 - 89]	87 [82 - 90]	86 [81 - 91]
Bilirubin, mg/dL	0.64 [0.41 - 0.99]	0.64 [0.41 - 0.94]	0.53 [0.35 - 0.76]	1.5 [0.88 - 2.7]	0.53 [0.35 - 0.94]	0.64 [0.41 - 0.99]	0.53 [0.35 - 0.76]	0.64 [0.47 - 0.94]	0.99 [0.58 - 1.9]
BUN, mg/dL	23 [16 - 35]	17 [13 - 23]	37 [27 - 55]	26 [18 - 39]	27 [17 - 39]	16 [12 - 22]	36 [27 - 55]	21 [15 - 30]	37 [26 - 54]
Chloride, mmol/L	99 (5.7)	99 (4.5)	100 (6.1)	97 (5.8)	101 (8.5)	100 (4.7)	100 (5.6)	97 (5.0)	101 (8.0)
Creatinine, mg/dL	1.1 [0.81 - 1.7]	0.89 [0.71 - 1.2]	1.7 [1.2 - 2.6]	1.2 [0.96 - 1.8]	1.2 [0.90 - 1.9]	0.88 [0.69 - 1.1]	1.7 [1.3 - 2.7]	1.0 [0.77 - 1.4]	1.7 [1.2 - 2.3]
CRP, mg/L	82 [30 - 180]	58 [22 - 133]	139 [69 - 239]	124 [56 - 235]	27 [5.9 - 79]	30 [12 - 81]	91 [38 - 175]	178 [100 - 280]	81 [36 - 186]
Erythrocyte Sedimentation Rate, mm/h	40 [21 - 71]	34 [18 - 57]	68 [43 - 99]	38 [16 - 65]	16 [7.3 - 33]	21 [11 - 35]	59 [38 - 89]	65 [44 - 95]	26 [11 - 53]
GCS	14 (2.6)	14 (1.3)	14 (1.5)	14 (2.1)	8.5 (4.5)	14 (2.7)	14 (1.5)	14 (1.5)	11 (4.2)
Glucose, mg/dL	130 [110 - 169]	128 [110 - 159]	126 [106 - 160]	132 [108 - 173]	195 [146 - 268]	126 [110 - 162]	128 [108 - 166]	133 [110 - 168]	147 [114 - 200]
Hemoglobin, g/dL	13 (2.2)	13 (1.7)	11 (1.7)	13 (2.4)	14 (2.3)	14 (1.6)	11 (1.8)	12 (1.9)	13 (2.7)
Heart rate, 1/min	107 (23)	109 (20)	99 (21)	116 (24)	111 (27)	107 (20)	94 (20)	116 (20)	113 (26)
INR	1.1 [1.0 - 1.3]	1.1 [1.0 - 1.2]	1.1 [1.0 - 1.2]	1.3 [1.2 - 1.5]	1.1 [1.0 - 1.2]	1.1 [1.0 - 1.2]	1.1 [1.0 - 1.2]	1.2 [1.1 - 1.3]	1.2 [1.1 - 1.4]
Lactate, mg/dL	15 [10 - 24]	13 [9.0 - 18]	14 [9.9 - 21]	29 [20 - 44]	34 [19 - 56]	13 [9.0 - 21]	13 [9.0 - 18]	16 [12 - 24]	36 [23 - 60]
Leucocytes, x10^3/µL	12 [8.7 - 17]	12 [8.9 - 16]	13 [9.3 - 18]	8.8 [3.7 - 14]	15 [11 - 20]	11 [8.3 - 15]	12 [8.5 - 16]	14 [9.3 - 19]	14 [8.6 - 20]
paO2, mmHg	74 (38)	66 (22)	72 (24)	75 (29)	121 (87)	72 (34)	72 (22)	66 (22)	100 (74)
Respiratory rate, 1/min	29 (11)	29 (9.8)	27 (7.0)	31 (9.1)	31 (25)	28 (7.3)	26 (6.4)	32 (18)	30 (8.9)
SpO2, %	93 [90 - 96]	93 [90 - 95]	94 [90 - 97]	94 [90 - 97]	94 [89 - 99]	93 [90 - 96]	94 [91 - 97]	93 [89 - 95]	94 [88 - 97]
SBP, mmHg	118 [96 - 140]	130 [110 - 150]	104 [89 - 125]	99 [86 - 120]	108 [85 - 134]	130 [109 - 151]	118 [98 - 139]	111 [93 - 132]	96 [80 - 115]
Sodium, mmol/L	138 (5.8)	138 (4.5)	139 (6.5)	136 (5.4)	141 (8.5)	139 (4.6)	139 (5.9)	136 (5.1)	141 (8.2)
Temperature, °C	37.7 (1.5)	38.2 (1.1)	37.4 (1.4)	37.8 (1.5)	36.2 (2.5)	38.0 (1.4)	37.5 (1.6)	38.1 (1.2)	36.8 (2.0)

Variable	Total	Phenotype							
		oslo				seneca			
		1os	2os	3os	4os	alpha	beta	gamma	delta
Thrombocytes, x10^9/L	229 [171 - 296]	226 [178 - 284]	259 [189 - 331]	147 [95 - 207]	258 [211 - 324]	219 [169 - 268]	238 [180 - 304]	245 [183 - 327]	204 [139 - 288]
Troponin, ng/mL	0.037 [0.022 - 0.065]	0.027 [0.018 - 0.040]	0.056 [0.036 - 0.094]	0.045 [0.024 - 0.069]	0.051 [0.028 - 0.099]	0.026 [0.015 - 0.037]	0.050 [0.033 - 0.084]	0.037 [0.024 - 0.061]	0.070 [0.045 - 0.18]
28-Day mortality no. (%)	337 (19%)	77 (9%)	133 (25%)	68 (30%)	59 (35%)	60 (10%)	86 (19%)	89 (18%)	102 (44%)
365-Day mortality no. (%)	681 (38%)	225 (26%)	270 (51%)	106 (46%)	80 (47%)	134 (21%)	211 (47%)	198 (40%)	138 (59%)

eSupplementary Table 4 Characteristics of the four phenotypes derived from applying the same consensus clustering approach on the Oxford cohort (1ox, 2ox, 3ox, 4ox), and the characteristics of the four phenotypes when Oxford patients are assigned to the closest SENECA phenotypes in Euclidean space. Data source: Oxford, Variable set: 29v. Expressed as median [IQR], mean (SD), or no. (%).

		Phenotype							
		oxford				seneca			
Variable	Total	1ox	2ox	3ox	4ox	alpha	beta	gamma	delta
No. of patients (%)	15575 (100%)	6273 (40%)	5715 (37%)	1198 (8%)	2389 (15%)	5206 (33%)	4145 (27%)	4348 (28%)	1876 (12%)
Age, years	71 (18)	71 (19)	76 (14)	61 (18)	68 (18)	66 (20)	78 (14)	72 (16)	72 (17)
Sex, male no. (%)	9067 (58%)	3665 (58%)	3425 (60%)	637 (53%)	1340 (56%)	3067 (59%)	2483 (60%)	2377 (55%)	1140 (61%)
ALAT, IU/L	26 [16 - 51]	22 [15 - 34]	22 [15 - 37]	31 [19 - 54]	157 [82 - 309]	26 [17 - 49]	19 [13 - 30]	26 [17 - 47]	99 [42 - 279]
Albumin, g/dL	3.2 (0.59)	3.4 (0.49)	3 (0.57)	3.2 (0.58)	3.1 (0.64)	3.5 (0.46)	3.1 (0.54)	2.9 (0.58)	3.1 (0.62)
Bands, %	85 [78 - 90]	85 [78 - 89]	87 [82 - 91]	59 [23 - 77]	87 [81 - 91]	83 [74 - 89]	84 [77 - 89]	87 [82 - 91]	88 [83 - 92]
Bilirubin, mg/dL	1.1 [0.64 - 1.8]	1.1 [0.64 - 1.6]	0.76 [0.53 - 1.2]	1.1 [0.64 - 1.6]	2.9 [1.6 - 5.1]	1.2 [0.70 - 2]	0.70 [0.47 - 1.1]	1.1 [0.70 - 1.7]	1.8 [0.88 - 3.8]
BUN, mg/dL	29 [18 - 49]	21 [15 - 29]	52 [37 - 74]	20 [14 - 29]	25 [17 - 39]	18 [13 - 24]	52 [37 - 75]	29 [21 - 42]	40 [25 - 64]
Chloride, mmol/L	105 (6.3)	104 (5.7)	106 (7.2)	103 (4.3)	104 (6.1)	104 (5.2)	105 (6.4)	103 (5.7)	109 (8.7)
Creatinine, mg/dL	1.4 [0.94 - 2.2]	1.1 [0.81 - 1.4]	2.3 [1.6 - 3.7]	0.98 [0.76 - 1.3]	1.2 [0.86 - 1.8]	0.96 [0.76 - 1.3]	2.4 [1.7 - 4.1]	1.3 [0.94 - 1.9]	1.7 [1.2 - 2.8]
CRP, mg/L	124 [53 - 217]	78 [24 - 160]	177 [102 - 266]	123 [62 - 213]	125 [61 - 210]	59 [19 - 124]	119 [58 - 201]	211 [142 - 295]	137 [68 - 220]
Erythrocyte Sedimentation Rate, mm/h	41 [20 - 72]	23 [11 - 43]	70 [43 - 88]	57 [35 - 85]	35 [16 - 61]	19 [11 - 35]	57 [36 - 85]	68 [43 - 86]	30 [14 - 55]
GCS	14 (2.3)	13 (2.7)	14 (2.1)	15 (0.92)	14 (2.1)	14 (2.6)	14 (1.5)	14 (1.9)	13 (3.4)
Glucose, mg/dL	142 [122 - 184]	133 [119 - 159]	166 [133 - 225]	124 [112 - 146]	142 [121 - 180]	128 [115 - 151]	153 [126 - 202]	150 [124 - 193]	159 [128 - 226]
Hemoglobin, g/dL	11 (2.5)	13 (2)	10 (2.1)	8.4 (2.1)	12 (2.4)	13 (2.3)	10 (2.1)	10 (2.3)	11 (2.6)
Heart rate, 1/min	97 (21)	93 (21)	97 (21)	101 (19)	103 (22)	94 (19)	86 (17)	106 (20)	107 (24)
INR	1.1 [1.1 - 1.3]	1.1 [1.0 - 1.2]	1.2 [1.1 - 1.3]	1.1 [1.1 - 1.2]	1.2 [1.1 - 1.6]	1.1 [1.0 - 1.2]	1.1 [1.1 - 1.3]	1.2 [1.1 - 1.3]	1.3 [1.1 - 1.8]
Lactate, mg/dL	17 [14 - 24]	16 [13 - 21]	18 [14 - 25]	14 [12 - 17]	24 [17 - 37]	16 [13 - 21]	15 [12 - 19]	18 [14 - 25]	35 [24 - 54]
Leucocytes, x10^3/µL	14 [9.4 - 19]	13 [9.2 - 17]	15 [11 - 21]	5.0 [1.9 - 11]	15 [11 - 21]	12 [8.0 - 16]	13 [9.0 - 17]	16 [11 - 22]	17 [12 - 23]
paO2, mmHg	66 (19)	66 (18)	67 (22)	65 (15)	66 (17)	66 (17)	67 (20)	64 (13)	71 (31)
Respiratory rate, 1/min	21 (5.4)	21 (5.1)	22 (5.8)	20 (3.9)	22 (5.8)	20 (4.3)	20 (3.6)	23 (6)	24 (7.1)
SpO2, %	95 [94 - 97]	95 [94 - 97]	95 [93 - 97]	96 [94 - 97]	95 [94 - 97]	96 [94 - 98]	96 [94 - 97]	94 [92 - 96]	95 [93 - 97]
SBP, mmHg	113 [99 - 132]	121 [105 - 140]	108 [94 - 126]	108 [97 - 120]	110 [97 - 125]	122 [108 - 140]	119 [104 - 138]	102 [91 - 116]	104 [90 - 120]
Sodium, mmol/L	138 (6.0)	138 (5.3)	138 (7)	136 (4.1)	136 (5.6)	138 (5.0)	138 (6.1)	137 (5.4)	140 (8.5)
Temperature, °C	37.1 (1.1)	37.1 (1.1)	37.0 (1.1)	37.7 (1.0)	37.1 (1.1)	37.2 (1.0)	36.7 (1.0)	37.5 (1.0)	36.9 (1.2)

		Phenotype							
		oxford				seneca			
Variable	Total	1ox	2ox	3ox	4ox	alpha	beta	gamma	delta
Thrombocytes, x10^9/L	186 [128 - 252]	192 [141 - 251]	207 [151 - 275]	40 [13 - 74]	175 [117 - 239]	177 [122 - 238]	205 [149 - 271]	184 [120 - 257]	175 [116 - 239]
Troponin, ng/mL	0.059 [0.039 - 0.090]	0.050 [0.032 - 0.080]	0.064 [0.040 - 0.11]	0.041 [0.029 - 0.060]	0.060 [0.040 - 0.11]	0.050 [0.030 - 0.080]	0.060 [0.040 - 0.098]	0.052 [0.037 - 0.085]	0.090 [0.050 - 0.29]
ASAT, IU/L	27 [19 - 50]	24 [19 - 33]	24 [18 - 34]	27 [19 - 44]	160 [87 - 300]	27 [20 - 48]	21 [18 - 30]	27 [19 - 43]	124 [51 - 291]
Bicarbonate, mmol/L	22 (3.7)	24 (2.7)	21 (4.1)	24 (2.4)	22 (4)	24 (2.3)	22 (3.9)	23 (3.2)	19 (4.8)
Elixhauser	2.8 (2)	2.2 (1.7)	3.7 (2.1)	2.2 (1.7)	2.8 (1.9)	2.0 (1.6)	3.8 (2.1)	2.8 (1.8)	3.1 (1.9)
28-Day mortality no. (%)	1875 (12%)	590 (9%)	832 (15%)	107 (9%)	346 (14%)	372 (7%)	599 (14%)	518 (12%)	386 (21%)
365-Day mortality no. (%)	4377 (28%)	1263 (20%)	1944 (34%)	429 (36%)	741 (31%)	884 (17%)	1421 (34%)	1380 (32%)	692 (37%)

eSupplementary Table 5 Characteristics of the four phenotypes derived from applying the same consensus clustering approach on the Stockholm cohort (1st, 2st, 3st, 4st), and the characteristics of the four phenotypes when Stockholm patients are assigned to the closest SENECA phenotypes in Euclidean space. Data source: Stockholm, Variable set: 29v. Expressed as median [IQR], mean (SD), or no. (%).

		Phenotype							
		stockholm				seneca			
Variable	Total	1st	2st	3st	4st	alpha	beta	gamma	delta
No. of patients (%)	30865 (100%)	14083 (46%)	9231 (30%)	4537 (15%)	3014 (10%)	10637 (34%)	7878 (26%)	8512 (28%)	3838 (12%)
Age, years	68 (16)	67 (16)	76 (12)	58 (16)	68 (16)	62 (18)	75 (13)	69 (14)	73 (15)
Sex, male no. (%)	18184 (59%)	7999 (57%)	5776 (63%)	2551 (56%)	1858 (62%)	6427 (60%)	4922 (62%)	4438 (52%)	2397 (62%)
ALAT, IU/L	25 [18 - 38]	23 [18 - 33]	21 [16 - 28]	30 [20 - 46]	107 [59 - 224]	28 [20 - 40]	20 [16 - 27]	23 [17 - 32]	60 [31 - 146]
Albumin, g/dL	2.9 (0.53)	3.1 (0.47)	2.6 (0.49)	2.9 (0.48)	2.8 (0.60)	3.3 (0.38)	2.8 (0.42)	2.6 (0.45)	2.7 (0.57)
Bands, %	82 [76 - 86]	83 [78 - 86]	83 [79 - 87]	50 [25 - 81]	84 [80 - 87]	81 [72 - 85]	82 [76 - 86]	83 [78 - 87]	84 [80 - 87]
Bilirubin, mg/dL	0.70 [0.47 - 1.1]	0.70 [0.53 - 0.94]	0.58 [0.41 - 0.82]	0.70 [0.53 - 0.99]	2.2 [1.2 - 4.1]	0.76 [0.53 - 1.1]	0.58 [0.41 - 0.82]	0.64 [0.47 - 0.94]	1.2 [0.64 - 2.6]
BUN, mg/dL	25 [17 - 36]	20 [15 - 26]	42 [33 - 55]	17 [14 - 23]	27 [20 - 37]	17 [13 - 21]	38 [29 - 52]	24 [18 - 30]	34 [25 - 49]
Chloride, mmol/L	103 (6.1)	102 (4.9)	106 (7.6)	102 (4.0)	103 (6.0)	103 (4.6)	104 (6.1)	102 (5.6)	107 (8.6)
Creatinine, mg/dL	1.2 [0.83 - 1.7]	0.98 [0.76 - 1.3]	2.0 [1.4 - 3.1]	0.85 [0.69 - 1.1]	1.2 [0.87 - 1.8]	0.89 [0.71 - 1.1]	1.9 [1.3 - 3]	1.0 [0.77 - 1.4]	1.6 [1.1 - 2.5]
CRP, mg/L	104 [44 - 201]	96 [36 - 190]	145 [73 - 244]	73 [36 - 142]	90 [33 - 180]	48 [18 - 104]	118 [63 - 203]	187 [111 - 282]	101 [40 - 200]
Erythrocyte Sedimentation Rate, mm/h	55 [33 - 83]	49 [28 - 78]	70 [43 - 88]	61 [39 - 84]	36 [19 - 61]	35 [22 - 52]	72 [48 - 88]	83 [62 - 95]	34 [20 - 56]
GCS	15 (1.7)	15 (1.4)	14 (2.1)	15 (0.56)	14 (2.1)	15 (1.4)	15 (1.0)	15 (1.1)	13 (3.2)
Glucose, mg/dL	137 [115 - 178]	137 [117 - 169]	153 [123 - 211]	123 [108 - 144]	142 [117 - 191]	130 [112 - 157]	141 [117 - 186]	142 [119 - 184]	159 [124 - 220]
Hemoglobin, g/dL	11 (2.3)	13 (1.9)	11 (2.0)	9.1 (1.8)	12 (2.4)	12 (2.4)	11 (2)	11 (2.1)	12 (2.5)
Heart rate, 1/min	106 (22)	107 (21)	104 (24)	104 (20)	108 (25)	104 (19)	93 (18)	117 (21)	113 (26)
INR	1.1 [1.1 - 1.3]	1.1 [1.1 - 1.2]	1.2 [1.1 - 1.3]	1.1 [1.0 - 1.2]	1.3 [1.2 - 1.7]	1.1 [1.0 - 1.2]	1.1 [1.1 - 1.2]	1.2 [1.1 - 1.3]	1.3 [1.1 - 1.6]
Lactate, mg/dL	14 [11 - 23]	14 [9.9 - 18]	17 [12 - 28]	12 [9.9 - 15]	27 [16 - 47]	13 [9.9 - 17]	13 [9.9 - 17]	16 [12 - 23]	34 [22 - 56]
Leucocytes, x10^3/µL	12 [7.0 - 16]	12 [8.9 - 16]	14 [9.6 - 19]	0.70 [0.20 - 2.2]	12 [8.3 - 18]	9.8 [4.1 - 14]	12 [8.2 - 16]	13 [7.7 - 18]	14 [9.1 - 19]
paO2, mmHg	77 (27)	69 (18)	82 (33)	85 (22)	85 (40)	74 (21)	80 (25)	71 (20)	90 (48)
Respiratory rate, 1/min	26 (7.9)	26 (7.8)	26 (8.3)	21 (5.3)	26 (8.3)	24 (7.1)	23 (6.0)	29 (8.2)	29 (9.0)
SpO2, %	93 [89 - 95]	91 [88 - 94]	93 [88 - 95]	96 [94 - 98]	94 [90 - 96]	93 [90 - 95]	94 [91 - 96]	91 [87 - 94]	92 [87 - 95]
SBP, mmHg	111 [97 - 129]	116 [100 - 131]	105 [90 - 123]	113 [100 - 126]	108 [92 - 125]	119 [104 - 132]	118 [101 - 134]	104 [90 - 120]	100 [85 - 118]
Sodium, mmol/L	137 (5.8)	137 (4.6)	139 (7.6)	136 (3.9)	136 (5.9)	138 (4.3)	138 (5.9)	136 (5.2)	140 (8.8)
Temperature, °C	38.2 (1.1)	38.5 (1.0)	37.7 (1.2)	38.5 (0.9)	37.9 (1.3)	38.5 (1.0)	37.8 (1.1)	38.4 (1.0)	37.6 (1.4)

		Phenotype							
		stockholm				seneca			
Variable	Total	1st	2st	3st	4st	alpha	beta	gamma	delta
Thrombocytes, x10^9/L	205 [131 - 284]	224 [165 - 296]	236 [171 - 318]	32 [12 - 78]	194 [129 - 269]	175 [97 - 247]	218 [151 - 295]	232 [148 - 327]	204 [136 - 281]
Troponin, ng/mL	0.032 [0.022 - 0.049]	0.027 [0.020 - 0.038]	0.047 [0.033 - 0.070]	0.024 [0.017 - 0.032]	0.042 [0.026 - 0.075]	0.024 [0.017 - 0.033]	0.039 [0.028 - 0.058]	0.033 [0.023 - 0.046]	0.057 [0.035 - 0.10]
ASAT, IU/L	30 [23 - 44]	29 [23 - 38]	29 [23 - 40]	25 [19 - 33]	148 [87 - 281]	29 [23 - 40]	26 [21 - 34]	30 [23 - 41]	93 [48 - 216]
Bicarbonate, mmol/L	24 (3.7)	25 (2.8)	22 (4.1)	25 (2.2)	22 (4.6)	25 (2.4)	23 (3.6)	25 (3.4)	20 (4.8)
Elixhauser	2.6 (2)	2 (1.6)	3.7 (2.2)	2.1 (1.4)	2.7 (1.9)	1.7 (1.5)	3.6 (2.1)	2.6 (1.8)	2.9 (2.0)
28-Day mortality no. (%)	4394 (14%)	1191 (8%)	2104 (23%)	352 (8%)	747 (25%)	532 (5%)	999 (13%)	1579 (19%)	1284 (33%)
365-Day mortality no. (%)	11655 (38%)	3777 (27%)	4714 (51%)	1704 (38%)	1460 (48%)	2318 (22%)	3203 (41%)	3948 (46%)	2186 (57%)

eSupplementary Table 6 Highlight table of Pearson correlation coefficients between scaled variable values and phenotype assignment of the Oslo cohort using phenotypes derived from each site where 26 variables were available (Oslo, Oxford, Stockholm, SENECA). Correlation coefficients are shaded blue when positive, red when negative. Higher absolute values are shaded with greater intensities of their respective color. Data source: Oslo, Variable set: 26v

	Oslo				Oxford				Stockholm				SENECA			
variable	1os	2os	3os	4os	1ox	2ox	3ox	4ox	1st	2st	3st	4st	alpha	beta	gamma	delta
Age	-0.12	0.24	-0.11	-0.06	-0.23	0.22	-0.17	0.10	-0.19	0.22	-0.20	0.11	-0.20	0.25	-0.04	0.02
Sex, male	-0.09	0.02	0.10	0.02	-0.07	0.03	0.01	0.05	-0.02	-0.01	-0.03	0.07	-0.04	0.04	-0.05	0.08
ALAT	-0.20	-0.16	0.38	0.14	-0.01	-0.21	0.07	0.22	-0.00	-0.16	0.06	0.19	-0.05	-0.20	-0.07	0.42
Albumin	0.47	-0.40	-0.27	0.11	0.51	-0.36	-0.17	-0.09	0.55	-0.40	-0.15	-0.09	0.56	-0.11	-0.34	-0.20
Bilirubin	-0.13	-0.20	0.53	-0.06	0.00	-0.21	0.10	0.19	0.03	-0.10	0.07	0.06	-0.03	-0.20	-0.02	0.32
BUN	-0.53	0.49	0.07	0.07	-0.52	0.40	-0.07	0.18	-0.47	0.35	-0.11	0.26	-0.47	0.43	-0.13	0.28
Chloride	-0.03	0.06	-0.12	0.08	-0.01	-0.12	-0.10	0.20	0.03	-0.18	-0.07	0.28	0.04	0.10	-0.23	0.11
Creatinine	-0.45	0.46	0.03	0.02	-0.41	0.40	-0.05	0.04	-0.38	0.31	-0.06	0.13	-0.38	0.45	-0.17	0.18
CRP	-0.20	0.29	0.13	-0.27	-0.40	0.30	0.08	0.08	-0.37	0.41	0.02	-0.08	-0.46	0.07	0.41	0.02
ESR	-0.14	0.39	-0.07	-0.28	-0.43	0.45	0.09	-0.08	-0.40	0.51	0.03	-0.18	-0.46	0.28	0.36	-0.19
GCS	0.24	0.12	0.04	-0.65	0.04	0.18	0.04	-0.29	0.09	0.20	0.04	-0.46	0.00	0.12	0.13	-0.33
Glucose	-0.10	-0.09	-0.00	0.32	-0.11	-0.02	0.00	0.15	-0.06	-0.06	-0.03	0.19	-0.07	-0.02	-0.01	0.13
Hemoglobin	0.32	-0.48	-0.01	0.22	0.40	-0.45	-0.18	0.16	0.44	-0.42	-0.19	0.12	0.44	-0.30	-0.23	0.07
Heart rate	0.07	-0.23	0.16	0.06	-0.01	-0.27	0.11	0.28	0.11	-0.20	0.05	0.11	0.01	-0.34	0.25	0.10
INR	-0.13	-0.05	0.34	-0.08	-0.10	-0.02	0.03	0.14	-0.05	0.00	0.02	0.06	-0.13	-0.06	0.00	0.25
Lactate	-0.33	-0.09	0.32	0.34	-0.21	-0.17	0.04	0.44	-0.18	-0.16	0.03	0.49	-0.16	-0.21	0.01	0.48
Leucocytes	0.00	0.13	-0.29	0.13	-0.04	0.11	-0.39	0.13	0.01	0.19	-0.47	0.06	-0.11	-0.03	0.11	0.05
paO2	-0.21	-0.03	0.01	0.40	-0.00	-0.02	0.03	0.01	-0.11	-0.07	0.06	0.23	-0.04	-0.03	-0.13	0.26
Resp. rate	0.01	-0.09	0.06	0.06	-0.08	-0.14	-0.03	0.29	0.01	-0.10	-0.05	0.17	-0.05	-0.13	0.15	0.04
SpO2	0.14	-0.05	-0.06	-0.09	-0.06	-0.06	-0.10	0.21	0.08	-0.02	-0.19	0.06	0.01	-0.12	0.13	-0.04
SBP	0.38	-0.21	-0.22	-0.08	0.30	-0.13	-0.06	-0.17	0.32	-0.12	-0.09	-0.22	0.27	0.02	-0.10	-0.29
Sodium	-0.01	0.01	-0.13	0.15	-0.01	-0.17	-0.16	0.31	0.04	-0.21	-0.13	0.37	0.05	0.06	-0.23	0.16
Temperature	0.28	-0.12	0.02	-0.32	0.09	-0.13	0.09	-0.00	0.20	-0.07	0.08	-0.25	0.11	-0.10	0.15	-0.23

	Oslo				Oxford				Stockholm				SENECA			
variable	**1os**	**2os**	**3os**	**4os**	**1ox**	**2ox**	**3ox**	**4ox**	**1st**	**2st**	**3st**	**4st**	**alpha**	**beta**	**gamma**	**delta**
Thrombocytes	0.05	0.19	-0.41	0.09	-0.00	0.17	-0.50	0.06	0.03	0.21	-0.49	0.03	-0.04	0.05	0.10	-0.15
Troponin T	-0.21	0.13	0.02	0.14	-0.17	0.04	-0.06	0.19	-0.17	0.00	-0.04	0.29	-0.17	0.01	-0.08	0.34
Bands	0.05	0.08	-0.17	-0.03	0.02	0.10	-0.38	0.07	0.05	0.11	-0.33	0.01	-0.07	-0.05	0.09	0.04

eSupplementary Table 7 Highlight table of Pearson correlation coefficients between scaled variable values and phenotype assignment of the Oxford cohort using phenotypes derived from sites where 29 variables were available (Oxford, Stockholm, SENECA). Correlation coefficients are shaded blue when positive, red when negative. Higher absolute values are shaded with greater intensities of their respective color. Data source: Oxford, Variable set: 29v

	Oxford				Stockholm				SENECA			
variable	1ox	2ox	3ox	4ox	1st	2st	3st	4st	alpha	beta	gamma	delta
Age	-0.04	0.21	-0.17	-0.09	-0.03	0.20	-0.21	-0.06	-0.23	0.21	0.03	0.01
Sex, male	0.00	0.03	-0.03	-0.02	-0.02	0.04	-0.03	-0.01	0.01	0.02	-0.04	0.02
ALAT	-0.27	-0.24	0.01	0.69	-0.22	-0.21	0.00	0.64	-0.00	-0.27	-0.06	0.46
Albumin	0.34	-0.29	-0.00	-0.08	0.31	-0.28	-0.01	-0.06	0.42	-0.11	-0.28	-0.07
Bilirubin	-0.09	-0.32	-0.02	0.57	-0.06	-0.30	-0.02	0.55	0.08	-0.30	-0.00	0.29
BUN	-0.44	0.62	-0.16	-0.11	-0.43	0.64	-0.21	-0.07	-0.55	0.50	-0.02	0.15
Chloride	-0.08	0.17	-0.07	-0.07	-0.17	0.26	-0.08	-0.03	-0.04	0.03	-0.14	0.21
Creatinine	-0.39	0.57	-0.16	-0.11	-0.42	0.60	-0.18	-0.06	-0.44	0.52	-0.13	0.10
CRP	-0.34	0.31	0.03	0.04	-0.13	0.19	-0.06	-0.03	-0.43	0.02	0.39	0.05
ESR	-0.44	0.43	0.12	-0.06	-0.26	0.30	0.08	-0.11	-0.51	0.26	0.36	-0.10
GCS	-0.13	0.02	0.12	0.05	-0.05	-0.04	0.12	0.03	-0.05	0.11	0.07	-0.16
Glucose	-0.23	0.31	-0.13	-0.01	-0.17	0.28	-0.16	0.00	-0.26	0.10	0.07	0.14
Hemoglobin	0.48	-0.34	-0.33	0.05	0.40	-0.27	-0.30	0.06	0.41	-0.21	-0.24	0.02
Heart rate	-0.13	0.00	0.06	0.12	-0.03	-0.03	0.01	0.08	-0.09	-0.31	0.27	0.18
INR	-0.16	0.11	-0.06	0.11	-0.15	0.10	-0.07	0.15	-0.18	0.00	0.03	0.22
Lactate	-0.17	0.04	-0.13	0.28	-0.22	0.12	-0.14	0.31	-0.17	-0.21	0.03	0.49
Leucocytes	-0.06	0.18	-0.34	0.09	0.08	0.16	-0.46	0.08	-0.18	-0.04	0.12	0.15
paO2	-0.01	0.03	-0.01	-0.01	-0.11	0.07	0.05	0.02	-0.02	0.02	-0.07	0.10
Resp. rate	-0.07	0.09	-0.08	0.04	-0.01	0.08	-0.13	0.02	-0.18	-0.19	0.22	0.21
SpO2	-0.06	0.10	-0.05	-0.01	0.11	0.01	-0.16	-0.04	-0.12	-0.11	0.22	0.02
SBP	0.25	-0.17	-0.07	-0.06	0.18	-0.14	-0.04	-0.05	0.25	0.13	-0.29	-0.15
Sodium	0.00	0.10	-0.06	-0.10	-0.05	0.17	-0.09	-0.08	0.01	0.02	-0.11	0.12
Temperature	-0.01	-0.07	0.15	-0.00	0.15	-0.18	0.09	-0.05	0.05	-0.22	0.23	-0.09
Thrombocytes	0.15	0.20	-0.63	-0.01	0.19	0.19	-0.60	-0.01	-0.07	0.13	-0.03	-0.02
Troponin T	-0.09	0.06	-0.06	0.08	-0.13	0.09	-0.07	0.14	-0.11	-0.05	-0.07	0.32
Bands	0.09	0.16	-0.56	0.08	0.12	0.12	-0.46	0.06	-0.13	-0.01	0.09	0.08
ASAT	-0.28	-0.25	-0.05	0.74	-0.26	-0.19	-0.04	0.72	-0.03	-0.26	-0.10	0.53
Bicarbonate	0.33	-0.35	0.10	-0.06	0.39	-0.42	0.11	-0.10	0.30	-0.15	0.09	-0.34
Elixhauser	-0.26	0.31	-0.09	-0.01	-0.27	0.33	-0.08	0.01	-0.29	0.30	-0.02	0.05

eSupplementary Table 8 Highlight table of Pearson correlation coefficients between scaled variable values and phenotype assignment of the Stockholm cohort using phenotypes derived from sites where 29 variables were available (Oxford, Stockholm, SENECA). Correlation coefficients are shaded blue when positive, red when negative. Higher absolute values are shaded with greater intensities of their respective color. Data source: Stockholm, Variable set: 29v

	Oxford				Stockholm				SENECA			
variable	**1ox**	**2ox**	**3ox**	**4ox**	**1st**	**2st**	**3st**	**4st**	**alpha**	**beta**	**gamma**	**delta**
Age	-0.10	0.30	-0.23	-0.05	-0.08	0.30	-0.26	-0.01	-0.31	0.23	0.03	0.10
Sex, male	-0.01	0.02	-0.02	0.01	-0.04	0.05	-0.02	0.02	0.02	0.04	-0.08	0.03
ALAT	-0.18	-0.28	0.04	0.64	-0.18	-0.24	0.06	0.61	0.04	-0.25	-0.14	0.45
Albumin	0.43	-0.37	0.01	-0.12	0.34	-0.32	0.02	-0.09	0.54	-0.09	-0.37	-0.15
Bilirubin	-0.12	-0.24	-0.04	0.57	-0.14	-0.21	-0.04	0.59	-0.00	-0.20	-0.08	0.38
BUN	-0.45	0.64	-0.25	-0.01	-0.44	0.66	-0.27	0.03	-0.56	0.51	-0.07	0.22
Chloride	-0.06	0.18	-0.10	-0.06	-0.16	0.27	-0.10	-0.01	-0.04	0.07	-0.19	0.21
Creatinine	-0.34	0.52	-0.22	-0.03	-0.37	0.57	-0.23	0.01	-0.38	0.47	-0.18	0.17
CRP	-0.27	0.30	-0.05	0.01	-0.09	0.20	-0.08	-0.06	-0.43	0.10	0.37	-0.01
ESR	-0.29	0.32	0.10	-0.13	-0.10	0.18	0.08	-0.20	-0.41	0.23	0.39	-0.23
GCS	-0.01	-0.05	0.10	-0.01	0.07	-0.13	0.11	-0.04	0.05	0.07	0.07	-0.26
Glucose	-0.11	0.21	-0.15	0.01	-0.07	0.19	-0.16	0.02	-0.17	0.04	0.04	0.13
Hemoglobin	0.45	-0.20	-0.41	0.05	0.41	-0.16	-0.41	0.05	0.29	-0.15	-0.18	0.03
Heart rate	-0.04	-0.01	-0.00	0.07	0.06	-0.06	-0.03	0.03	-0.06	-0.34	0.31	0.11
INR	-0.13	0.06	-0.09	0.19	-0.12	0.06	-0.10	0.24	-0.15	-0.02	-0.02	0.27
Lactate	-0.20	0.10	-0.15	0.31	-0.23	0.16	-0.17	0.33	-0.21	-0.20	0.03	0.51
Leucocytes	0.15	0.26	-0.67	0.09	0.25	0.24	-0.73	0.08	-0.21	0.07	0.07	0.12
paO2	-0.14	0.04	0.09	0.05	-0.25	0.12	0.12	0.10	-0.06	0.07	-0.14	0.19
Resp. rate	0.00	0.11	-0.20	0.04	0.09	0.08	-0.24	0.03	-0.16	-0.21	0.24	0.18
SpO2	0.14	0.10	-0.31	-0.04	0.26	0.03	-0.37	-0.05	-0.09	-0.14	0.21	0.04
SBP	0.19	-0.16	0.01	-0.06	0.18	-0.17	0.02	-0.06	0.19	0.13	-0.20	-0.19
Sodium	0.04	0.11	-0.11	-0.10	-0.05	0.18	-0.12	-0.06	0.03	0.06	-0.18	0.14
Temperature	0.15	-0.21	0.13	-0.04	0.22	-0.27	0.12	-0.09	0.20	-0.22	0.13	-0.18
Thrombocytes	0.21	0.27	-0.73	0.04	0.30	0.23	-0.73	0.02	-0.20	0.08	0.10	0.04
Troponin T	-0.14	0.11	-0.09	0.14	-0.16	0.12	-0.10	0.19	-0.16	0.01	-0.06	0.30
Bands	0.16	0.18	-0.58	0.09	0.18	0.15	-0.51	0.08	-0.12	-0.03	0.09	0.09
ASAT	-0.20	-0.17	-0.17	0.71	-0.18	-0.13	-0.17	0.70	-0.12	-0.21	-0.10	0.58
Bicarbonate	0.28	-0.26	0.11	-0.14	0.34	-0.34	0.11	-0.19	0.23	-0.08	0.12	-0.38
Elixhauser	-0.29	0.36	-0.09	0.00	-0.28	0.37	-0.10	0.02	-0.32	0.31	-0.01	0.06

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References

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