## Supplementary Table 1. Basic demographic characteristics of the original cohort

|  | **Optimal TWA-MAP (N=7421) 1** | **Low TWA-MAP (N=4441) 2** | **High TWA-MAP (N=1174) 3** | **p-value** | **SMD (Compare to Optimal TWA-MAP, respectively)** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- | --- |
| Age | **66.15 (14.27)** | **70.24 (13.72)** | **61.70 (15.13)** | **<0.001** | **[ 0.292 , 0.303 ]** | **0.00** |
| Gender (Female) | **2804 (37.78%)** | **1848 (41.61%)** | **474 (40.37%)** | **<0.001** | **[ 0.078 , 0.053 ]** | **0.00** |
| Weight | **84.01 (24.59)** | **82.91 (32.16)** | **83.03 (23.43)** | **<0.01** | **[ 0.038 , 0.041 ]** | **0.00** |
| SAPS II | **42.69 (14.26)** | **45.26 (14.27)** | **38.30 (13.91)** | **<0.001** | **[ 0.180 , 0.312 ]** | **0.00** |
| SOFA score | **8.13 (3.85)** | **8.46 (3.94)** | **7.12 (3.63)** | **<0.001** | **[ 0.085 , 0.269 ]** | **0.00** |
| Charlson comorbidity index | **5.80 (2.73)** | **6.71 (2.74)** | **5.06 (2.70)** | **<0.001** | **[ 0.331 , 0.275 ]** | **0.00** |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** | | | | | |  |
| Mechanical ventilation (YES) | **4425 (59.63%)** | **2263 (50.96%)** | **681 (58.01%)** | **<0.001** | **[ 0.175 , 0.033 ]** | **0.00** |
| Sedative therapy (YES) | **5902 (79.53%)** | **3014 (67.87%)** | **969 (82.54%)** | **<0.001** | **[ 0.267 , 0.077 ]** | **0.00** |
| Length of vasopressor therapy | **41.31 (59.81)** | **45.12 (68.11)** | **17.67 (33.66)** | **<0.001** | **[ 0.059 , 0.487 ]** | **0.00** |
| **Comorbidities (boolean)** | | | | | |  |
| HF (YES) | **2372 (31.96%)** | **1713 (38.57%)** | **304 (25.89%)** | **<0.001** | **[ 0.139 , 0.134 ]** | **0.00** |
| Hypertension (YES) | 4984 (67.16%) | 2998 (67.51%) | 750 (63.88%) | 0.06 | [ 0.007 , 0.069 ] | 0.00 |
| AFIB (YES) | **1642 (22.13%)** | **1115 (25.11%)** | **224 (19.08%)** | **<0.001** | **[ 0.070 , 0.075 ]** | **0.00** |
| Renal (YES) | **1596 (21.51%)** | **1374 (30.94%)** | **194 (16.52%)** | **<0.001** | **[ 0.216 , 0.127 ]** | **0.00** |
| Liver (YES) | **472 (6.36%)** | **442 (9.95%)** | **52 (4.43%)** | **<0.001** | **[ 0.132 , 0.086 ]** | **0.00** |
| COPD (YES) | **1162 (15.66%)** | **753 (16.96%)** | **122 (10.39%)** | **<0.001** | **[ 0.035 , 0.157 ]** | **0.00** |
| CAD (YES) | **3014 (40.61%)** | **1917 (43.17%)** | **400 (34.07%)** | **<0.001** | **[ 0.052 , 0.136 ]** | **0.00** |
| Stroke (YES) | **569 (7.67%)** | **279 (6.28%)** | **192 (16.35%)** | **<0.001** | **[ 0.054 , 0.270 ]** | **0.00** |
| Malignancy (YES) | **1302 (17.54%)** | **844 (19.00%)** | **168 (14.31%)** | **<0.001** | **[ 0.038 , 0.088 ]** | **0.00** |
| **Vital signs (1st 24 h)** | | | | | |  |
| MAP | **79.38 (17.65)** | **73.19 (17.95)** | **88.11 (16.67)** | **<0.001** | **[ 0.348 , 0.508 ]** | **0.00** |
| Temperature | **36.48 (2.82)** | **36.58 (1.81)** | **36.24 (2.96)** | **<0.001** | **[ 0.040 , 0.085 ]** | **8.21** |
| Heart rate | **91.02 (20.70)** | **88.90 (19.32)** | **88.82 (20.35)** | **<0.001** | **[ 0.106 , 0.107 ]** | **0.00** |
| **Laboratory tests (1st 24 h)** | | | | | |  |
| pH | **7.35 (0.10)** | **7.36 (0.10)** | **7.37 (0.09)** | **<0.001** | **[ 0.017 , 0.126 ]** | **9.57** |
| PO2 | **217.61 (126.84)** | **208.22 (126.54)** | **235.23 (126.52)** | **<0.001** | **[ 0.074 , 0.139 ]** | **19.76** |
| PCO2 | **42.53 (11.03)** | **42.25 (11.04)** | **41.92 (11.06)** | **<0.05** | **[ 0.025 , 0.055 ]** | **10.74** |
| Lactate | 2.64 (2.06) | 2.67 (2.25) | 2.54 (1.90) | 0.47 | [ 0.012 , 0.051 ] | 9.52 |
| Creatinine | **1.51 (1.52)** | **1.82 (1.68)** | **1.33 (1.38)** | **<0.001** | **[ 0.195 , 0.125 ]** | **0.20** |
| WBC | **14.45 (9.49)** | **14.37 (9.43)** | **13.39 (7.06)** | **<0.05** | **[ 0.008 , 0.127 ]** | **0.39** |
| Hemoglobin | **10.16 (2.23)** | **9.70 (1.99)** | **10.68 (2.36)** | **<0.001** | **[ 0.219 , 0.224 ]** | **0.35** |
| Platelet | 195.65 (111.55) | 196.98 (114.62) | 195.31 (100.63) | 0.31 | [ 0.012 , 0.003 ] | 0.42 |
| **Outcomes (boolean)** | | | | | |  |
| 28-day mortality (Death) | **1254 (16.90%)** | **1147 (25.83%)** | **179 (15.25%)** | **<0.001** | **[ 0.219 , 0.045 ]** | **0.00** |
| ICU mortality (Death) | **826 (11.13%)** | **766 (17.25%)** | **114 (9.71%)** | **<0.001** | **[ 0.176 , 0.046 ]** | **0.00** |
| **Length of Stay (days)** | | | | | |  |
| ICU LOS | **5.79 (6.63)** | **5.12 (5.70)** | **5.11 (6.23)** | **<0.001** | **[ 0.108 , 0.106 ]** | **0.00** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | | |
| 2Low TWA-MAP: TWA-MAP < 70 (mm Hg) | | | | | | |
| 3High TWA-MAP: 83 ≤ TWA-MAP (mm Hg) | | | | | | |

## Supplementary Table 2. Standardized mean difference (SMD) of covariates before and after propensity score matching of cohort 1

| Characteristic | Before matcing | After matcing |
| --- | --- | --- |
| SMD ≤ 0.1 | 17 | 29 |
| SMD > 0.1 | 12 | 0 |
| Total number of covariates | 29 | 29 |

## Supplementary Table 3. Baseline characteristics before propensity score matching of cohort 1

|  | **Optimal TWA-MAP (N=7421) 1** | **Low TWA-MAP (N=4441) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | **66.15 (14.27)** | **70.24 (13.72)** | **<0.001** | **0.292** | **0** |
| Gender (Female) | **2804 (37.78%)** | **1848 (41.61%)** | **<0.001** | **0.078** | **0** |
| Weight | **84.01 (24.59)** | **82.91 (32.16)** | **<0.001** | **0.038** | **0** |
| SAPS II | **42.69 (14.26)** | **45.26 (14.27)** | **<0.001** | **0.18** | **0** |
| SOFA score | **8.13 (3.85)** | **8.46 (3.94)** | **<0.001** | **0.085** | **0** |
| Charlson comorbidity index | **5.80 (2.73)** | **6.71 (2.74)** | **<0.001** | **0.331** | **0** |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | **4425 (59.63%)** | **2263 (50.96%)** | **<0.001** | **0.175** | **0** |
| Sedative therapy (YES) | **5902 (79.53%)** | **3014 (67.87%)** | **<0.001** | **0.267** | **0** |
| Length of vasopressor therapy | **41.31 (59.81)** | **45.12 (68.11)** | **<0.001** | **0.059** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | **2372 (31.96%)** | **1713 (38.57%)** | **<0.001** | **0.139** | **0** |
| Hypertension (YES) | 4984 (67.16%) | 2998 (67.51%) | 0.71 | 0.007 | 0 |
| AFIB (YES) | **1642 (22.13%)** | **1115 (25.11%)** | **<0.001** | **0.07** | **0** |
| Renal (YES) | **1596 (21.51%)** | **1374 (30.94%)** | **<0.001** | **0.216** | **0** |
| Liver (YES) | **472 (6.36%)** | **442 (9.95%)** | **<0.001** | **0.132** | **0** |
| COPD (YES) | 1162 (15.66%) | 753 (16.96%) | 0.07 | 0.035 | 0 |
| CAD (YES) | **3014 (40.61%)** | **1917 (43.17%)** | **<0.01** | **0.052** | **0** |
| Stroke (YES) | **569 (7.67%)** | **279 (6.28%)** | **<0.01** | **0.054** | **0** |
| Malignancy (YES) | **1302 (17.54%)** | **844 (19.00%)** | **<0.05** | **0.038** | **0** |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **79.38 (17.65)** | **73.19 (17.95)** | **<0.001** | **0.348** | **0** |
| Temperature | 36.47 (2.90) | 36.57 (1.77) | 0.07 | 0.04 | 0 |
| Heart rate | **91.02 (20.70)** | **88.90 (19.32)** | **<0.001** | **0.106** | **0** |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | 7.35 (0.10) | 7.36 (0.10) | 0.25 | 0.029 | 0 |
| PO2 | **215.97 (126.08)** | **205.73 (125.92)** | **<0.001** | **0.081** | **0** |
| PCO2 | 42.54 (11.03) | 42.21 (10.89) | 0.05 | 0.03 | 0 |
| Lactate | 2.64 (2.07) | 2.64 (2.19) | 0.3 | 0.003 | 0 |
| Creatinine | **1.51 (1.51)** | **1.82 (1.68)** | **<0.001** | **0.195** | **0** |
| WBC | 14.44 (9.48) | 14.37 (9.41) | 0.82 | 0.008 | 0 |
| Hemoglobin | **10.16 (2.23)** | **9.70 (1.99)** | **<0.001** | **0.219** | **0** |
| Platelet | 195.76 (111.53) | 196.88 (114.52) | 0.63 | 0.01 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | **1254 (16.90%)** | **1147 (25.83%)** | **<0.001** | **0.219** | **0** |
| ICU mortality (Death) | **826 (11.13%)** | **766 (17.25%)** | **<0.001** | **0.176** | **0** |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | **5.79 (6.63)** | **5.12 (5.70)** | **<0.01** | **0.108** | **0** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2Low TWA-MAP: TWA-MAP < 70 (mm Hg) | | | | | |

## Supplementary Table 4. Baseline characteristics after propensity score matching of cohort 1

|  | **Optimal TWA-MAP (N=4027) 1** | **Low TWA-MAP (N=4027) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | 69.54 (13.46) | 69.70 (13.78) | 0.23 | 0.012 | 0 |
| Gender (Female) | 1644 (40.82%) | 1635 (40.60%) | 0.86 | 0.005 | 0 |
| Weight | 82.57 (23.10) | 83.03 (25.54) | 0.54 | 0.019 | 0 |
| SAPS II | 44.73 (14.27) | 44.67 (14.18) | 0.97 | 0.004 | 0 |
| SOFA score | 8.34 (3.84) | 8.34 (3.94) | 0.77 | 0.002 | 0 |
| Charlson comorbidity index | 6.52 (2.71) | 6.50 (2.69) | 0.93 | 0.007 | 0 |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | 2150 (53.39%) | 2162 (53.69%) | 0.81 | 0.006 | 0 |
| Sedative therapy (YES) | 2861 (71.05%) | 2900 (72.01%) | 0.35 | 0.021 | 0 |
| Length of vasopressor therapy | 43.47 (62.71) | 43.12 (60.56) | 0.45 | 0.006 | 0 |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | 1487 (36.93%) | 1487 (36.93%) | 1 | <0.001 | 0 |
| Hypertension (YES) | 2714 (67.40%) | 2753 (68.36%) | 0.36 | 0.021 | 0 |
| AFIB (YES) | 968 (24.04%) | 995 (24.71%) | 0.5 | 0.016 | 0 |
| Renal (YES) | 1156 (28.71%) | 1134 (28.16%) | 0.6 | 0.012 | 0 |
| Liver (YES) | 357 (8.87%) | 340 (8.44%) | 0.53 | 0.015 | 0 |
| COPD (YES) | 678 (16.84%) | 675 (16.76%) | 0.95 | 0.002 | 0 |
| CAD (YES) | 1688 (41.92%) | 1735 (43.08%) | 0.3 | 0.024 | 0 |
| Stroke (YES) | 281 (6.98%) | 266 (6.61%) | 0.54 | 0.015 | 0 |
| Malignancy (YES) | 741 (18.40%) | 750 (18.62%) | 0.82 | 0.006 | 0 |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **75.04 (15.87)** | **74.61 (17.83)** | **<0.001** | **0.026** | **0** |
| Temperature | 36.49 (3.31) | 36.56 (1.84) | 0.15 | 0.029 | 0 |
| Heart rate | 89.81 (20.23) | 89.51 (19.44) | 0.87 | 0.015 | 0 |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | 7.36 (0.10) | 7.36 (0.10) | 0.37 | 0.011 | 0 |
| PO2 | 208.72 (125.81) | 210.46 (126.52) | 0.63 | 0.014 | 0 |
| PCO2 | 42.27 (11.20) | 42.23 (10.77) | 0.89 | 0.003 | 0 |
| Lactate | 2.66 (2.09) | 2.65 (2.19) | 0.17 | 0.005 | 0 |
| Creatinine | 1.72 (1.76) | 1.69 (1.55) | 0.6 | 0.014 | 0 |
| WBC | 14.36 (9.58) | 14.42 (9.53) | 0.45 | 0.006 | 0 |
| Hemoglobin | 9.82 (2.13) | 9.77 (2.01) | 0.48 | 0.023 | 0 |
| Platelet | 197.69 (116.69) | 196.89 (113.48) | 0.62 | 0.007 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | **797 (19.79%)** | **981 (24.36%)** | **<0.001** | **0.11** | **0** |
| ICU mortality (Death) | **481 (11.94%)** | **669 (16.61%)** | **<0.001** | **0.134** | **0** |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | **5.75 (6.51)** | **5.13 (5.66)** | **<0.01** | **0.101** | **0** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2Low TWA-MAP: TWA-MAP < 70 (mm Hg) | | | | | |

## Supplementary Table 5. Standardized mean difference (SMD) of covariates before and after propensity score matching of cohort 2

| Characteristic | Before matcing | After matcing |
| --- | --- | --- |
| SMD ≤ 0.1 | 12 | 29 |
| SMD > 0.1 | 17 | 0 |
| Total number of covariates | 29 | 29 |

## Supplementary Table 6. Baseline characteristics before propensity score matching of cohort 2

|  | **Optimal TWA-MAP (N=7421) 1** | **High TWA-MAP (N=1174) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | **66.15 (14.27)** | **61.70 (15.13)** | **<0.001** | **0.303** | **0** |
| Gender (Female) | 2804 (37.78%) | 474 (40.37%) | 0.1 | 0.053 | 0 |
| Weight | 84.01 (24.59) | 83.03 (23.43) | 0.13 | 0.041 | 0 |
| SAPS II | **42.69 (14.26)** | **38.30 (13.91)** | **<0.001** | **0.312** | **0** |
| SOFA score | **8.13 (3.85)** | **7.12 (3.63)** | **<0.001** | **0.269** | **0** |
| Charlson comorbidity index | **5.80 (2.73)** | **5.06 (2.70)** | **<0.001** | **0.275** | **0** |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | 4425 (59.63%) | 681 (58.01%) | 0.31 | 0.033 | 0 |
| Sedative therapy (YES) | **5902 (79.53%)** | **969 (82.54%)** | **<0.05** | **0.077** | **0** |
| Length of vasopressor therapy | **41.31 (59.81)** | **17.67 (33.66)** | **<0.001** | **0.487** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | **2372 (31.96%)** | **304 (25.89%)** | **<0.001** | **0.134** | **0** |
| Hypertension (YES) | **4984 (67.16%)** | **750 (63.88%)** | **<0.05** | **0.069** | **0** |
| AFIB (YES) | **1642 (22.13%)** | **224 (19.08%)** | **<0.05** | **0.075** | **0** |
| Renal (YES) | **1596 (21.51%)** | **194 (16.52%)** | **<0.001** | **0.127** | **0** |
| Liver (YES) | **472 (6.36%)** | **52 (4.43%)** | **<0.05** | **0.086** | **0** |
| COPD (YES) | **1162 (15.66%)** | **122 (10.39%)** | **<0.001** | **0.157** | **0** |
| CAD (YES) | **3014 (40.61%)** | **400 (34.07%)** | **<0.001** | **0.136** | **0** |
| Stroke (YES) | **569 (7.67%)** | **192 (16.35%)** | **<0.001** | **0.27** | **0** |
| Malignancy (YES) | **1302 (17.54%)** | **168 (14.31%)** | **<0.01** | **0.088** | **0** |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **79.38 (17.65)** | **88.11 (16.67)** | **<0.001** | **0.508** | **0** |
| Temperature | **36.47 (2.90)** | **36.25 (2.88)** | **<0.01** | **0.076** | **0** |
| Heart rate | **91.02 (20.70)** | **88.82 (20.35)** | **<0.001** | **0.107** | **0** |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | **7.35 (0.10)** | **7.37 (0.10)** | **<0.001** | **0.118** | **0** |
| PO2 | **215.97 (126.08)** | **229.45 (126.71)** | **<0.001** | **0.107** | **0** |
| PCO2 | 42.54 (11.03) | 42.08 (11.11) | 0.11 | 0.041 | 0 |
| Lactate | 2.64 (2.07) | 2.54 (1.85) | 0.49 | 0.051 | 0 |
| Creatinine | **1.51 (1.51)** | **1.33 (1.38)** | **<0.001** | **0.124** | **0** |
| WBC | **14.44 (9.48)** | **13.39 (7.05)** | **<0.01** | **0.127** | **0** |
| Hemoglobin | **10.16 (2.23)** | **10.67 (2.36)** | **<0.001** | **0.221** | **0** |
| Platelet | 195.76 (111.53) | 195.36 (100.47) | 0.12 | 0.004 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | 1254 (16.90%) | 179 (15.25%) | 0.17 | 0.045 | 0 |
| ICU mortality (Death) | 826 (11.13%) | 114 (9.71%) | 0.16 | 0.046 | 0 |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | **5.79 (6.63)** | **5.11 (6.23)** | **<0.001** | **0.106** | **0** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2High TWA-MAP: 83 ≤ TWA-MAP (mm Hg) | | | | | |

## Supplementary Table 7. Baseline characteristics after propensity score matching of cohort 2

|  | **Optimal TWA-MAP (N=1167) 1** | **High TWA-MAP (N=1167) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | 62.07 (15.95) | 61.70 (15.13) | 0.39 | 0.024 | 0 |
| Gender (Female) | 452 (38.73%) | 471 (40.36%) | 0.45 | 0.033 | 0 |
| Weight | 83.24 (24.04) | 82.96 (23.38) | 0.97 | 0.012 | 0 |
| SAPS II | 38.09 (13.10) | 38.26 (13.90) | 0.91 | 0.013 | 0 |
| SOFA score | 7.02 (3.54) | 7.12 (3.63) | 0.54 | 0.028 | 0 |
| Charlson comorbidity index | 5.01 (2.76) | 5.05 (2.70) | 0.7 | 0.017 | 0 |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | 664 (56.90%) | 680 (58.27%) | 0.53 | 0.028 | 0 |
| Sedative therapy (YES) | 958 (82.09%) | 962 (82.43%) | 0.87 | 0.009 | 0 |
| Length of vasopressor therapy | **18.87 (26.93)** | **17.72 (33.75)** | **<0.001** | **0.038** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | 294 (25.19%) | 302 (25.88%) | 0.74 | 0.016 | 0 |
| Hypertension (YES) | 717 (61.44%) | 744 (63.75%) | 0.27 | 0.048 | 0 |
| AFIB (YES) | 226 (19.37%) | 223 (19.11%) | 0.92 | 0.007 | 0 |
| Renal (YES) | 209 (17.91%) | 193 (16.54%) | 0.41 | 0.036 | 0 |
| Liver (YES) | 57 (4.88%) | 52 (4.46%) | 0.69 | 0.02 | 0 |
| COPD (YES) | 115 (9.85%) | 122 (10.45%) | 0.68 | 0.02 | 0 |
| CAD (YES) | 381 (32.65%) | 399 (34.19%) | 0.46 | 0.033 | 0 |
| Stroke (YES) | 180 (15.42%) | 185 (15.85%) | 0.82 | 0.012 | 0 |
| Malignancy (YES) | 161 (13.80%) | 167 (14.31%) | 0.77 | 0.015 | 0 |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **87.48 (20.14)** | **87.92 (16.36)** | **<0.001** | **0.024** | **0** |
| Temperature | 36.13 (4.24) | 36.25 (2.89) | 0.5 | 0.031 | 0 |
| Heart rate | 88.99 (20.34) | 88.85 (20.38) | 0.88 | 0.007 | 0 |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | 7.37 (0.09) | 7.36 (0.10) | 0.72 | 0.016 | 0 |
| PO2 | 227.53 (130.65) | 229.79 (126.88) | 0.5 | 0.017 | 0 |
| PCO2 | 42.08 (10.05) | 42.12 (11.11) | 0.5 | 0.004 | 0 |
| Lactate | 2.51 (1.85) | 2.54 (1.86) | 0.64 | 0.016 | 0 |
| Creatinine | 1.32 (1.35) | 1.33 (1.38) | 0.8 | 0.007 | 0 |
| WBC | 13.47 (7.08) | 13.37 (7.05) | 0.66 | 0.015 | 0 |
| Hemoglobin | 10.68 (2.30) | 10.66 (2.35) | 0.78 | 0.012 | 0 |
| Platelet | 194.12 (105.79) | 194.99 (100.53) | 0.28 | 0.008 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | **128 (10.97%)** | **175 (15.00%)** | **<0.01** | **0.12** | **0** |
| ICU mortality (Death) | 85 (7.28%) | 112 (9.60%) | 0.05 | 0.083 | 0 |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | 4.79 (5.41) | 5.11 (6.25) | 0.81 | 0.055 | 0 |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2High TWA-MAP: 83 ≤ TWA-MAP (mm Hg) | | | | | |

## Supplementary Table 8. Generalized additive model for 28-day mortality of cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.41 | 1.27, 1.56 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.84 | 0.76, 0.94 | 0.002 |
| Weight | 0.99 | 0.99, 0.99 | <0.001 |
| SAPS II | 1.03 | 1.03, 1.03 | <0.001 |
| SOFA score | 1.20 | 1.18, 1.22 | <0.001 |
| Charlson comorbidity index | 1.12 | 1.10, 1.14 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.48 | 1.32, 1.65 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 9. Piece-wise exponential additive mixed model for 28-day mortality of cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.49 | 1.37, 1.61 | <0.001 |
| Age | 1.01 | 1.01, 1.01 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.86 | 0.79, 0.94 | <0.001 |
| Weight | 0.99 | 0.99, 0.99 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.19 | 1.17, 1.21 | <0.001 |
| Charlson comorbidity index | 1.09 | 1.07, 1.10 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.41 | 1.29, 1.54 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 10. Survey-weighted generalised linear model with all covariates using IPW for 28-day mortality of cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.49 | 1.33, 1.67 | <0.001 |
| Age | 1.02 | 1.02, 1.03 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.92 | 0.81, 1.05 | 0.2 |
| Weight | 0.99 | 0.99, 1.00 | 0.019 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.19 | 1.16, 1.22 | <0.001 |
| Charlson comorbidity index | 1.11 | 1.07, 1.14 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.00 | 0.85, 1.17 | >0.9 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.69 | 1.42, 2.01 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.03 | 0.91, 1.17 | 0.6 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.30 | 1.14, 1.48 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.92, 1.20 | 0.5 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.12 | 0.96, 1.31 | 0.14 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.72 | 0.59, 0.87 | <0.001 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.78, 1.04 | 0.2 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.19 | 1.05, 1.35 | 0.008 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.55 | 0.45, 0.68 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.77 | 0.66, 0.89 | <0.001 |
| MAP | 1.00 | 1.00, 1.01 | 0.076 |
| Temperature | 0.99 | 0.97, 1.01 | 0.3 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.001 |
| pH | 1.12 | 0.56, 2.26 | 0.7 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.10 |
| Lactate | 1.08 | 1.05, 1.11 | <0.001 |
| Creatinine | 0.98 | 0.94, 1.02 | 0.2 |
| WBC | 1.00 | 1.00, 1.01 | 0.083 |
| Hemoglobin | 1.03 | 1.00, 1.06 | 0.053 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 11. Proportional hazards assumption for survey-weighted Cox model using IPW for 28-day mortality of cohort 1

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 0.99 |
| Age | 0.98 |
| Gender | 0.99 |
| Weight | 0.96 |
| SAPS II | 0.95 |
| SOFA score | 0.98 |
| Charlson comorbidity index | 0.96 |
| Mechanical ventilation | 0.98 |
| Sedative therapy | 0.99 |
| Length of vasopressor therapy | 0.90 |
| HF | 0.99 |
| Hypertension | 0.99 |
| AFIB | 0.98 |
| Renal | 0.98 |
| Liver | 0.98 |
| COPD | 1.00 |
| CAD | 0.99 |
| Stroke | 0.99 |
| Malignancy | 0.97 |
| MAP | 0.99 |
| Temperature | 0.98 |
| Heart rate | 0.99 |
| pH | 0.95 |
| PO2 | 0.99 |
| PCO2 | 0.99 |
| Lactate | 0.94 |
| Creatinine | 0.98 |
| WBC | 1.00 |
| Hemoglobin | 0.96 |
| Platelet | 0.99 |
| GLOBAL | 1.00 |

## Supplementary Table 12. Survey-weighted Cox model with all covariates using IPW for 28-day mortality of cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.51 | 1.37, 1.65 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.93 | 0.84, 1.03 | 0.2 |
| Weight | 0.99 | 0.99, 1.00 | 0.013 |
| SAPS II | 1.02 | 1.01, 1.02 | <0.001 |
| SOFA score | 1.15 | 1.13, 1.17 | <0.001 |
| Charlson comorbidity index | 1.08 | 1.05, 1.10 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.00 | 0.88, 1.14 | >0.9 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.47 | 1.28, 1.69 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.011 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.02 | 0.92, 1.13 | 0.7 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.23 | 1.11, 1.36 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.07 | 0.96, 1.20 | 0.2 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.11 | 0.99, 1.25 | 0.085 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.81 | 0.70, 0.94 | 0.005 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.92 | 0.82, 1.03 | 0.2 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.16 | 1.05, 1.28 | 0.005 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.68 | 0.58, 0.79 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.76, 0.96 | 0.007 |
| MAP | 1.00 | 1.00, 1.00 | 0.14 |
| Temperature | 0.99 | 0.98, 1.00 | 0.2 |
| Heart rate | 1.00 | 1.00, 1.01 | <0.001 |
| pH | 0.88 | 0.51, 1.53 | 0.7 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.088 |
| Lactate | 1.06 | 1.04, 1.08 | <0.001 |
| Creatinine | 0.99 | 0.96, 1.02 | 0.7 |
| WBC | 1.00 | 1.00, 1.01 | 0.054 |
| Hemoglobin | 1.03 | 1.01, 1.05 | 0.014 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 13. Cox model with all covariates using IPW for 28-day mortality of cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.50 | 1.37, 1.65 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.93 | 0.85, 1.03 | 0.2 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.44 | 1.25, 1.65 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.03 | 0.94, 1.13 | 0.5 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.23 | 1.11, 1.36 | <0.001 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.93 | 0.83, 1.03 | 0.2 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.16 | 1.05, 1.28 | 0.003 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.68 | 0.59, 0.79 | <0.001 |
| MAP | 1.00 | 1.00, 1.00 | 0.10 |
| Heart rate | 1.00 | 1.00, 1.01 | <0.001 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.059 |
| WBC | 1.00 | 1.00, 1.01 | 0.047 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| tt(Age) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(Weight) | 1.00 | 1.00, 1.00 | 0.005 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(SOFA score) | 1.04 | 1.04, 1.05 | <0.001 |
| tt(Charlson comorbidity index) | 1.02 | 1.02, 1.03 | <0.001 |
| tt(Mechanical ventilation) | 1.01 | 0.97, 1.04 | 0.7 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(AFIB) | 1.02 | 0.99, 1.05 | 0.3 |
| tt(Renal) | 1.03 | 1.00, 1.07 | 0.074 |
| tt(Liver) | 0.94 | 0.90, 0.98 | 0.002 |
| tt(Malignancy) | 0.95 | 0.92, 0.98 | 0.002 |
| tt(Temperature) | 1.00 | 0.99, 1.00 | 0.063 |
| tt(pH) | 0.98 | 0.84, 1.14 | 0.8 |
| tt(Lactate) | 1.02 | 1.01, 1.02 | <0.001 |
| tt(Creatinine) | 1.00 | 0.99, 1.01 | 0.6 |
| tt(Hemoglobin) | 1.01 | 1.00, 1.01 | 0.016 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 14. Generalized additive model for 28-day mortality of cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.44 | 1.19, 1.74 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.057 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.88 | 0.77, 1.01 | 0.059 |
| Weight | 0.99 | 0.98, 0.99 | <0.001 |
| SAPS II | 1.03 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.15 | 1.12, 1.17 | <0.001 |
| Charlson comorbidity index | 1.12 | 1.09, 1.15 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.21 | 1.06, 1.39 | 0.005 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 15. Piece-wise exponential additive mixed model for 28-day mortality of cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.32 | 1.12, 1.55 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.89 | 0.80, 1.00 | 0.046 |
| Weight | 0.99 | 0.99, 0.99 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.14 | 1.12, 1.16 | <0.001 |
| Charlson comorbidity index | 1.10 | 1.07, 1.12 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.19 | 1.06, 1.34 | 0.003 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 16. Survey-weighted generalised linear model with all covariates using IPW for 28-day mortality of cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.75 | 1.34, 2.27 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.96 | 0.83, 1.11 | 0.6 |
| Weight | 0.99 | 0.99, 0.99 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.16 | 1.13, 1.20 | <0.001 |
| Charlson comorbidity index | 1.11 | 1.07, 1.16 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.91 | 0.75, 1.11 | 0.4 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.96 | 1.58, 2.44 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.90, 1.23 | 0.5 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.32 | 1.13, 1.54 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.09 | 0.92, 1.29 | 0.3 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.12 | 0.91, 1.37 | 0.3 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.88 | 0.68, 1.14 | 0.3 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.84 | 0.71, 1.00 | 0.055 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.26 | 1.07, 1.48 | 0.006 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.44 | 0.35, 0.55 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.70, 1.02 | 0.073 |
| MAP | 1.00 | 1.00, 1.01 | 0.3 |
| Temperature | 0.99 | 0.97, 1.02 | 0.6 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.13 |
| pH | 1.92 | 0.82, 4.49 | 0.13 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.00, 1.02 | 0.006 |
| Lactate | 1.10 | 1.06, 1.13 | <0.001 |
| Creatinine | 0.96 | 0.91, 1.01 | 0.2 |
| WBC | 1.01 | 1.00, 1.01 | 0.041 |
| Hemoglobin | 1.04 | 1.01, 1.08 | 0.012 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 17. Proportional hazards assumption for survey-weighted Cox model using IPW for 28-day mortality of cohort 2

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 0.97 |
| Age | 0.96 |
| Gender | 0.99 |
| Weight | 0.97 |
| SAPS II | 0.96 |
| SOFA score | 0.99 |
| Charlson comorbidity index | 0.94 |
| Mechanical ventilation | 0.98 |
| Sedative therapy | 0.99 |
| Length of vasopressor therapy | 0.91 |
| HF | 0.98 |
| Hypertension | 0.99 |
| AFIB | 0.99 |
| Renal | 0.96 |
| Liver | 0.98 |
| COPD | 0.98 |
| CAD | 0.99 |
| Stroke | 1.00 |
| Malignancy | 0.97 |
| MAP | 0.98 |
| Temperature | 0.98 |
| Heart rate | 0.99 |
| pH | 0.97 |
| PO2 | 1.00 |
| PCO2 | 1.00 |
| Lactate | 0.95 |
| Creatinine | 0.99 |
| WBC | 1.00 |
| Hemoglobin | 0.95 |
| Platelet | 0.99 |
| GLOBAL | 1.00 |

## Supplementary Table 18. Survey-weighted Cox model with all covariates using IPW for 28-day mortality of cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.58 | 1.27, 1.97 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.95 | 0.84, 1.08 | 0.4 |
| Weight | 0.99 | 0.99, 0.99 | <0.001 |
| SAPS II | 1.02 | 1.01, 1.02 | <0.001 |
| SOFA score | 1.14 | 1.11, 1.16 | <0.001 |
| Charlson comorbidity index | 1.09 | 1.05, 1.12 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.92 | 0.78, 1.08 | 0.3 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.79 | 1.48, 2.16 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.04 | 0.91, 1.18 | 0.6 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.25 | 1.10, 1.42 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.08 | 0.94, 1.25 | 0.3 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.14 | 0.97, 1.34 | 0.11 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.73, 1.10 | 0.3 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.88 | 0.76, 1.02 | 0.079 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.19 | 1.04, 1.36 | 0.013 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.55 | 0.47, 0.66 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.78, 1.05 | 0.2 |
| MAP | 1.00 | 1.00, 1.00 | 0.6 |
| Temperature | 0.99 | 0.98, 1.01 | 0.4 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.082 |
| pH | 1.78 | 0.90, 3.52 | 0.10 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.00, 1.01 | <0.001 |
| Lactate | 1.07 | 1.05, 1.10 | <0.001 |
| Creatinine | 0.98 | 0.94, 1.02 | 0.3 |
| WBC | 1.00 | 1.00, 1.01 | 0.038 |
| Hemoglobin | 1.04 | 1.01, 1.07 | 0.003 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 19. Cox model with all covariates using IPW for 28-day mortality of cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.96 | 0.85, 1.08 | 0.5 |
| SOFA score | 1.14 | 1.11, 1.17 | <0.001 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.75 | 1.46, 2.10 | <0.001 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.25 | 1.11, 1.41 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.08 | 0.94, 1.24 | 0.3 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.89 | 0.77, 1.02 | 0.082 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.19 | 1.04, 1.36 | 0.011 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.55 | 0.47, 0.65 | <0.001 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.064 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.00, 1.01 | <0.001 |
| Creatinine | 0.98 | 0.94, 1.02 | 0.3 |
| WBC | 1.00 | 1.00, 1.01 | 0.041 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| tt(Group) | 1.14 | 1.08, 1.22 | <0.001 |
| tt(Age) | 1.00 | 1.00, 1.01 | <0.001 |
| tt(Weight) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(SAPS II) | 1.00 | 1.00, 1.01 | <0.001 |
| tt(Charlson comorbidity index) | 1.03 | 1.02, 1.03 | <0.001 |
| tt(Mechanical ventilation) | 0.98 | 0.94, 1.03 | 0.4 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(HF) | 1.01 | 0.97, 1.05 | 0.6 |
| tt(Renal) | 1.04 | 0.99, 1.09 | 0.12 |
| tt(Liver) | 0.96 | 0.91, 1.02 | 0.2 |
| tt(Malignancy) | 0.97 | 0.93, 1.01 | 0.10 |
| tt(MAP) | 1.00 | 1.00, 1.00 | 0.6 |
| tt(Temperature) | 1.00 | 0.99, 1.00 | 0.5 |
| tt(pH) | 1.19 | 0.99, 1.45 | 0.066 |
| tt(Lactate) | 1.02 | 1.01, 1.03 | <0.001 |
| tt(Hemoglobin) | 1.01 | 1.00, 1.02 | 0.004 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 20. Generalized additive model for ICU mortality of cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.48 | 1.31, 1.67 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.015 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.79 | 0.69, 0.89 | <0.001 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.03 | 1.03, 1.04 | <0.001 |
| SOFA score | 1.21 | 1.19, 1.24 | <0.001 |
| Charlson comorbidity index | 1.04 | 1.02, 1.07 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.04 | 0.91, 1.19 | 0.6 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 21. Piece-wise exponential additive mixed model for ICU mortality of cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.64 | 1.48, 1.81 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.88 | 0.79, 0.97 | 0.013 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.14 | 1.12, 1.16 | <0.001 |
| Charlson comorbidity index | 1.03 | 1.01, 1.05 | 0.004 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.38 | 1.23, 1.54 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 22. Survey-weighted generalised linear model with all covariates using IPW for ICU mortality of cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.70 | 1.49, 1.94 | <0.001 |
| Age | 1.01 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.85 | 0.74, 0.98 | 0.021 |
| Weight | 0.99 | 0.99, 1.00 | 0.001 |
| SAPS II | 1.03 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.19 | 1.16, 1.23 | <0.001 |
| Charlson comorbidity index | 1.05 | 1.01, 1.09 | 0.007 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.86 | 0.71, 1.04 | 0.11 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.36 | 1.10, 1.69 | 0.005 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.01 | 0.87, 1.17 | 0.9 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.29 | 1.12, 1.50 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.09 | 0.92, 1.28 | 0.3 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.15 | 0.95, 1.38 | 0.14 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.99 | 0.79, 1.25 | >0.9 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.83 | 0.70, 0.98 | 0.029 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.04 | 0.89, 1.21 | 0.7 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.49 | 0.39, 0.62 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.92 | 0.77, 1.09 | 0.3 |
| MAP | 1.00 | 1.00, 1.01 | 0.026 |
| Temperature | 0.98 | 0.96, 1.00 | 0.047 |
| Heart rate | 1.01 | 1.00, 1.01 | <0.001 |
| pH | 0.86 | 0.39, 1.88 | 0.7 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.00, 1.01 | 0.032 |
| Lactate | 1.11 | 1.08, 1.14 | <0.001 |
| Creatinine | 0.96 | 0.91, 1.00 | 0.053 |
| WBC | 1.00 | 0.99, 1.00 | 0.8 |
| Hemoglobin | 1.06 | 1.03, 1.09 | <0.001 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 23. Proportional hazards assumption for survey-weighted Cox model using IPW for ICU mortality of cohort 1

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 1.00 |
| Age | 0.99 |
| Gender | 0.98 |
| Weight | 0.99 |
| SAPS II | 0.93 |
| SOFA score | 0.95 |
| Charlson comorbidity index | 1.00 |
| Mechanical ventilation | 0.96 |
| Sedative therapy | 0.98 |
| Length of vasopressor therapy | 0.91 |
| HF | 0.98 |
| Hypertension | 0.99 |
| AFIB | 1.00 |
| Renal | 1.00 |
| Liver | 0.99 |
| COPD | 1.00 |
| CAD | 0.99 |
| Stroke | 1.00 |
| Malignancy | 1.00 |
| MAP | 0.98 |
| Temperature | 0.99 |
| Heart rate | 0.98 |
| pH | 0.95 |
| PO2 | 0.98 |
| PCO2 | 1.00 |
| Lactate | 0.96 |
| Creatinine | 0.98 |
| WBC | 1.00 |
| Hemoglobin | 0.97 |
| Platelet | 1.00 |
| GLOBAL | 1.00 |

## Supplementary Table 24. Survey-weighted Cox model with all covariates using IPW for ICU mortality of cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.73 | 1.54, 1.94 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.89 | 0.79, 1.00 | 0.050 |
| Weight | 1.00 | 0.99, 1.00 | 0.002 |
| SAPS II | 1.02 | 1.01, 1.03 | <0.001 |
| SOFA score | 1.09 | 1.07, 1.11 | <0.001 |
| Charlson comorbidity index | 1.04 | 1.01, 1.07 | 0.018 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.07 | 0.91, 1.25 | 0.4 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.49 | 1.24, 1.79 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 0.98 | 0.86, 1.11 | 0.8 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.25 | 1.10, 1.41 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.28 | 1.11, 1.47 | <0.001 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.22 | 1.05, 1.43 | 0.012 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.91 | 0.75, 1.09 | 0.3 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.94 | 0.81, 1.08 | 0.4 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.93 | 0.82, 1.06 | 0.3 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.71, 1.03 | 0.10 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.98 | 0.84, 1.14 | 0.8 |
| MAP | 1.00 | 1.00, 1.00 | 0.5 |
| Temperature | 0.98 | 0.96, 0.99 | 0.003 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.011 |
| pH | 0.76 | 0.39, 1.47 | 0.4 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.3 |
| Lactate | 1.08 | 1.06, 1.10 | <0.001 |
| Creatinine | 1.04 | 1.00, 1.07 | 0.050 |
| WBC | 1.00 | 1.00, 1.01 | 0.14 |
| Hemoglobin | 1.04 | 1.02, 1.07 | 0.002 |
| Platelet | 1.00 | 1.00, 1.00 | 0.8 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 25. Cox model with all covariates using IPW for ICU mortality of cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.72 | 1.54, 1.93 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Weight | 1.00 | 0.99, 1.00 | 0.001 |
| Charlson comorbidity index | 1.04 | 1.01, 1.07 | 0.011 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.24 | 1.10, 1.40 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.28 | 1.12, 1.46 | <0.001 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.22 | 1.06, 1.41 | 0.007 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.76, 1.06 | 0.2 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.93 | 0.82, 1.06 | 0.3 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.94 | 0.83, 1.06 | 0.3 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.72, 1.01 | 0.070 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.97 | 0.85, 1.11 | 0.7 |
| Temperature | 0.98 | 0.97, 0.99 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.2 |
| WBC | 1.00 | 1.00, 1.01 | 0.043 |
| Platelet | 1.00 | 1.00, 1.00 | 0.8 |
| tt(Gender) | 0.96 | 0.93, 1.00 | 0.027 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(SOFA score) | 1.03 | 1.02, 1.03 | <0.001 |
| tt(Mechanical ventilation) | 1.02 | 0.98, 1.07 | 0.3 |
| tt(Sedative therapy) | 1.13 | 1.07, 1.19 | <0.001 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(HF) | 0.99 | 0.96, 1.03 | 0.7 |
| tt(MAP) | 1.00 | 1.00, 1.00 | 0.4 |
| tt(Heart rate) | 1.00 | 1.00, 1.00 | 0.008 |
| tt(pH) | 0.94 | 0.79, 1.13 | 0.5 |
| tt(PO2) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(Lactate) | 1.02 | 1.02, 1.03 | <0.001 |
| tt(Creatinine) | 1.01 | 1.00, 1.02 | 0.046 |
| tt(Hemoglobin) | 1.01 | 1.00, 1.02 | 0.002 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 26. Generalized additive model for ICU mortality of cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.46 | 1.16, 1.83 | 0.001 |
| Age | 1.00 | 1.00, 1.01 | 0.6 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.81 | 0.69, 0.94 | 0.007 |
| Weight | 0.99 | 0.99, 0.99 | <0.001 |
| SAPS II | 1.03 | 1.03, 1.04 | <0.001 |
| SOFA score | 1.14 | 1.11, 1.17 | <0.001 |
| Charlson comorbidity index | 1.04 | 1.01, 1.07 | 0.017 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.89 | 0.75, 1.05 | 0.2 |
| Length of vasopressor therapy | 1.01 | 1.00, 1.01 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 27. Piece-wise exponential additive mixed model for ICU mortality of cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.26 | 1.03, 1.54 | 0.027 |
| Age | 1.01 | 1.00, 1.01 | 0.056 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.87 | 0.76, 1.00 | 0.053 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.08 | 1.06, 1.10 | <0.001 |
| Charlson comorbidity index | 1.03 | 1.00, 1.06 | 0.045 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.18 | 1.01, 1.37 | 0.034 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.002 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 28. Survey-weighted generalised linear model with all covariates using IPW for ICU mortality of cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.56 | 1.14, 2.13 | 0.005 |
| Age | 1.01 | 1.00, 1.02 | 0.011 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.83 | 0.70, 0.99 | 0.041 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.03 | 1.02, 1.04 | <0.001 |
| SOFA score | 1.15 | 1.11, 1.19 | <0.001 |
| Charlson comorbidity index | 1.05 | 1.01, 1.11 | 0.026 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.81 | 0.64, 1.03 | 0.089 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.45 | 1.09, 1.93 | 0.011 |
| Length of vasopressor therapy | 1.01 | 1.00, 1.01 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.87, 1.26 | 0.6 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.39 | 1.16, 1.67 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.04 | 0.85, 1.28 | 0.7 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.22 | 0.95, 1.56 | 0.11 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 1.15 | 0.83, 1.58 | 0.4 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.81 | 0.66, 1.00 | 0.049 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.10 | 0.90, 1.34 | 0.4 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.40 | 0.31, 0.51 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 1.00 | 0.80, 1.25 | >0.9 |
| MAP | 1.00 | 1.00, 1.01 | 0.2 |
| Temperature | 0.98 | 0.95, 1.00 | 0.079 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.14 |
| pH | 3.22 | 1.21, 8.56 | 0.019 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.01, 1.02 | <0.001 |
| Lactate | 1.12 | 1.08, 1.16 | <0.001 |
| Creatinine | 0.96 | 0.90, 1.02 | 0.2 |
| WBC | 1.00 | 1.00, 1.01 | 0.5 |
| Hemoglobin | 1.07 | 1.03, 1.11 | <0.001 |
| Platelet | 1.00 | 1.00, 1.00 | 0.002 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 29. Proportional hazards assumption for survey-weighted Cox model using IPW for ICU mortality of cohort 2

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 0.97 |
| Age | 0.98 |
| Gender | 0.97 |
| Weight | 0.99 |
| SAPS II | 0.95 |
| SOFA score | 0.96 |
| Charlson comorbidity index | 0.98 |
| Mechanical ventilation | 0.97 |
| Sedative therapy | 0.99 |
| Length of vasopressor therapy | 0.92 |
| HF | 0.97 |
| Hypertension | 0.99 |
| AFIB | 0.99 |
| Renal | 0.99 |
| Liver | 0.97 |
| COPD | 0.99 |
| CAD | 0.98 |
| Stroke | 0.98 |
| Malignancy | 0.99 |
| MAP | 0.97 |
| Temperature | 0.99 |
| Heart rate | 1.00 |
| pH | 0.95 |
| PO2 | 0.99 |
| PCO2 | 0.99 |
| Lactate | 0.96 |
| Creatinine | 0.98 |
| WBC | 0.99 |
| Hemoglobin | 0.96 |
| Platelet | 1.00 |
| GLOBAL | 1.00 |

## Supplementary Table 30. Survey-weighted Cox model with all covariates using IPW for ICU mortality of cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.38 | 1.02, 1.87 | 0.034 |
| Age | 1.01 | 1.00, 1.02 | 0.003 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.86 | 0.74, 1.00 | 0.047 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.07 | 1.04, 1.10 | <0.001 |
| Charlson comorbidity index | 1.04 | 1.00, 1.09 | 0.043 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.97 | 0.79, 1.19 | 0.8 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.85 | 1.44, 2.37 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.01 | 0.86, 1.19 | 0.9 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.30 | 1.11, 1.52 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.17 | 0.98, 1.39 | 0.089 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.37 | 1.10, 1.69 | 0.004 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.96 | 0.74, 1.26 | 0.8 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.76, 1.08 | 0.3 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.89 | 0.75, 1.05 | 0.2 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.76 | 0.61, 0.94 | 0.011 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 1.01 | 0.83, 1.22 | >0.9 |
| MAP | 1.00 | 1.00, 1.00 | >0.9 |
| Temperature | 0.98 | 0.96, 0.99 | 0.008 |
| Heart rate | 1.00 | 1.00, 1.00 | 0.7 |
| pH | 2.85 | 1.23, 6.61 | 0.015 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.00, 1.01 | 0.021 |
| Lactate | 1.09 | 1.06, 1.12 | <0.001 |
| Creatinine | 1.03 | 0.98, 1.08 | 0.2 |
| WBC | 1.00 | 1.00, 1.01 | 0.10 |
| Hemoglobin | 1.06 | 1.03, 1.09 | <0.001 |
| Platelet | 1.00 | 1.00, 1.00 | 0.7 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 31. Cox model with all covariates using IPW for ICU mortality of cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Age | 1.01 | 1.00, 1.02 | 0.001 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.80 | 1.41, 2.30 | <0.001 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.29 | 1.11, 1.50 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.17 | 0.98, 1.39 | 0.082 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.36 | 1.12, 1.66 | 0.002 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.91 | 0.76, 1.07 | 0.3 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.75 | 0.62, 0.92 | 0.006 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 1.00 | 0.84, 1.19 | >0.9 |
| Temperature | 0.98 | 0.96, 0.99 | 0.001 |
| Heart rate | 1.00 | 1.00, 1.00 | 0.6 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.01 | 1.00, 1.01 | 0.007 |
| WBC | 1.01 | 1.00, 1.01 | 0.007 |
| Platelet | 1.00 | 1.00, 1.00 | 0.8 |
| tt(Group) | 1.10 | 1.01, 1.19 | 0.025 |
| tt(Gender) | 0.95 | 0.91, 0.99 | 0.028 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(SOFA score) | 1.02 | 1.01, 1.03 | <0.001 |
| tt(Charlson comorbidity index) | 1.01 | 1.00, 1.02 | 0.028 |
| tt(Mechanical ventilation) | 0.99 | 0.94, 1.06 | 0.9 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | 0.002 |
| tt(HF) | 1.00 | 0.96, 1.05 | >0.9 |
| tt(Liver) | 0.98 | 0.91, 1.06 | 0.6 |
| tt(CAD) | 0.96 | 0.91, 1.01 | 0.14 |
| tt(MAP) | 1.00 | 1.00, 1.00 | 0.8 |
| tt(pH) | 1.41 | 1.12, 1.79 | 0.004 |
| tt(Lactate) | 1.03 | 1.02, 1.03 | <0.001 |
| tt(Creatinine) | 1.01 | 0.99, 1.02 | 0.2 |
| tt(Hemoglobin) | 1.02 | 1.01, 1.03 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 32. Basic demographic characteristics of the subgroup original cohort

|  | **Optimal TWA-MAP (N=3844) 1** | **Low TWA-MAP (N=4174) 2** | **High TWA-MAP (N=1006) 3** | **p-value** | **SMD (Compare to Optimal TWA-MAP, respectively)** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- | --- |
| Age | **65.13 (13.97)** | **70.25 (13.73)** | **61.59 (15.24)** | **<0.001** | **[ 0.369 , 0.242 ]** | **0.00** |
| Gender (Female) | **1308 (34.03%)** | **1749 (41.90%)** | **409 (40.66%)** | **<0.001** | **[ 0.163 , 0.137 ]** | **0.00** |
| Weight | **84.25 (22.70)** | **83.06 (32.76)** | **82.75 (23.60)** | **<0.001** | **[ 0.042 , 0.064 ]** | **0.00** |
| SAPS II | **40.83 (13.90)** | **45.33 (14.27)** | **38.47 (14.13)** | **<0.001** | **[ 0.319 , 0.169 ]** | **0.00** |
| SOFA score | **7.73 (3.74)** | **8.48 (3.94)** | **7.12 (3.64)** | **<0.001** | **[ 0.197 , 0.166 ]** | **0.00** |
| Charlson comorbidity index | **5.58 (2.69)** | **6.72 (2.73)** | **5.05 (2.72)** | **<0.001** | **[ 0.422 , 0.195 ]** | **0.00** |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** | | | | | |  |
| Mechanical ventilation (YES) | **2231 (58.04%)** | **2144 (51.37%)** | **581 (57.75%)** | **<0.001** | **[ 0.134 , 0.006 ]** | **0.00** |
| Sedative therapy (YES) | **3076 (80.02%)** | **2830 (67.80%)** | **823 (81.81%)** | **<0.001** | **[ 0.281 , 0.046 ]** | **0.00** |
| Length of vasopressor therapy | **34.11 (51.62)** | **46.81 (69.58)** | **17.76 (34.15)** | **<0.001** | **[ 0.207 , 0.374 ]** | **0.00** |
| **Comorbidities (boolean)** | | | | | |  |
| HF (YES) | **1183 (30.78%)** | **1616 (38.72%)** | **262 (26.04%)** | **<0.001** | **[ 0.167 , 0.105 ]** | **0.00** |
| Hypertension (YES) | **2559 (66.57%)** | **2812 (67.37%)** | **634 (63.02%)** | **<0.05** | **[ 0.017 , 0.074 ]** | **0.00** |
| AFIB (YES) | **834 (21.70%)** | **1046 (25.06%)** | **191 (18.99%)** | **<0.001** | **[ 0.080 , 0.067 ]** | **0.00** |
| Renal (YES) | **757 (19.69%)** | **1287 (30.83%)** | **164 (16.30%)** | **<0.001** | **[ 0.259 , 0.088 ]** | **0.00** |
| Liver (YES) | **236 (6.14%)** | **426 (10.21%)** | **46 (4.57%)** | **<0.001** | **[ 0.149 , 0.070 ]** | **0.00** |
| COPD (YES) | **516 (13.42%)** | **711 (17.03%)** | **103 (10.24%)** | **<0.001** | **[ 0.101 , 0.099 ]** | **0.00** |
| CAD (YES) | **1632 (42.46%)** | **1800 (43.12%)** | **332 (33.00%)** | **<0.001** | **[ 0.014 , 0.196 ]** | **0.00** |
| Stroke (YES) | **301 (7.83%)** | **261 (6.25%)** | **177 (17.59%)** | **<0.001** | **[ 0.062 , 0.296 ]** | **0.00** |
| Malignancy (YES) | **613 (15.95%)** | **791 (18.95%)** | **148 (14.71%)** | **<0.001** | **[ 0.079 , 0.034 ]** | **0.00** |
| **Vital signs (1st 24 h)** | | | | | |  |
| MAP | **79.49 (16.97)** | **73.09 (18.04)** | **88.32 (16.72)** | **<0.001** | **[ 0.366 , 0.525 ]** | **0.00** |
| Temperature | **36.49 (2.89)** | **36.58 (1.85)** | **36.21 (3.17)** | **<0.001** | **[ 0.037 , 0.092 ]** | **8.39** |
| Heart rate | **90.37 (19.92)** | **88.80 (19.27)** | **88.72 (20.39)** | **<0.01** | **[ 0.080 , 0.082 ]** | **0.00** |
| **Laboratory tests (1st 24 h)** | | | | | |  |
| pH | **7.36 (0.09)** | **7.36 (0.10)** | **7.37 (0.09)** | **<0.01** | **[ 0.032 , 0.082 ]** | **10.34** |
| PO2 | **227.66 (127.31)** | **207.39 (126.08)** | **231.61 (126.80)** | **<0.001** | **[ 0.160 , 0.031 ]** | **20.77** |
| PCO2 | **42.44 (10.34)** | **42.30 (11.12)** | **41.76 (10.78)** | **<0.05** | **[ 0.014 , 0.064 ]** | **11.66** |
| Lactate | 2.56 (1.88) | 2.67 (2.25) | 2.52 (1.88) | 0.82 | [ 0.053 , 0.020 ] | 9.98 |
| Creatinine | **1.43 (1.40)** | **1.82 (1.68)** | **1.32 (1.35)** | **<0.001** | **[ 0.254 , 0.080 ]** | **0.23** |
| WBC | **14.46 (8.72)** | **14.44 (9.56)** | **13.41 (7.08)** | **<0.01** | **[ 0.002 , 0.133 ]** | **0.43** |
| Hemoglobin | **10.21 (2.23)** | **9.68 (1.98)** | **10.67 (2.36)** | **<0.001** | **[ 0.249 , 0.202 ]** | **0.39** |
| Platelet | 192.65 (107.27) | 197.64 (115.37) | 195.23 (100.77) | 0.07 | [ 0.045 , 0.025 ] | 0.47 |
| **Outcomes (boolean)** | | | | | |  |
| 28-day mortality (Death) | **541 (14.07%)** | **1094 (26.21%)** | **156 (15.51%)** | **<0.001** | **[ 0.306 , 0.040 ]** | **0.00** |
| ICU mortality (Death) | **342 (8.90%)** | **733 (17.56%)** | **100 (9.94%)** | **<0.001** | **[ 0.258 , 0.036 ]** | **0.00** |
| **Length of Stay (days)** | | | | | |  |
| ICU LOS | **5.20 (6.37)** | **5.20 (5.77)** | **5.24 (6.45)** | **<0.001** | **[ <0.001 , 0.007 ]** | **0.00** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | | |
| 2Low TWA-MAP: TWA-MAP < 70 (mm Hg) | | | | | | |
| 3High TWA-MAP: 83 ≤ TWA-MAP (mm Hg) | | | | | | |

## Supplementary Table 33. Standardized mean difference (SMD) of covariates before and after propensity score matching of subgroup cohort 1

| Characteristic | Before matcing | After matcing |
| --- | --- | --- |
| SMD ≤ 0.1 | 13 | 29 |
| SMD > 0.1 | 16 | 0 |
| Total number of covariates | 29 | 29 |

## Supplementary Table 34. Baseline characteristics before propensity score matching of subgroup cohort 1

|  | **Optimal TWA-MAP (N=3844) 1** | **Low TWA-MAP (N=4174) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | **65.13 (13.97)** | **70.25 (13.73)** | **<0.001** | **0.369** | **0** |
| Gender (Female) | **1308 (34.03%)** | **1749 (41.90%)** | **<0.001** | **0.163** | **0** |
| Weight | **84.25 (22.70)** | **83.06 (32.76)** | **<0.001** | **0.042** | **0** |
| SAPS II | **40.83 (13.90)** | **45.33 (14.27)** | **<0.001** | **0.319** | **0** |
| SOFA score | **7.73 (3.74)** | **8.48 (3.94)** | **<0.001** | **0.197** | **0** |
| Charlson comorbidity index | **5.58 (2.69)** | **6.72 (2.73)** | **<0.001** | **0.422** | **0** |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | **2231 (58.04%)** | **2144 (51.37%)** | **<0.001** | **0.134** | **0** |
| Sedative therapy (YES) | **3076 (80.02%)** | **2830 (67.80%)** | **<0.001** | **0.281** | **0** |
| Length of vasopressor therapy | **34.11 (51.62)** | **46.81 (69.58)** | **<0.001** | **0.207** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | **1183 (30.78%)** | **1616 (38.72%)** | **<0.001** | **0.167** | **0** |
| Hypertension (YES) | 2559 (66.57%) | 2812 (67.37%) | 0.46 | 0.017 | 0 |
| AFIB (YES) | **834 (21.70%)** | **1046 (25.06%)** | **<0.001** | **0.08** | **0** |
| Renal (YES) | **757 (19.69%)** | **1287 (30.83%)** | **<0.001** | **0.259** | **0** |
| Liver (YES) | **236 (6.14%)** | **426 (10.21%)** | **<0.001** | **0.149** | **0** |
| COPD (YES) | **516 (13.42%)** | **711 (17.03%)** | **<0.001** | **0.101** | **0** |
| CAD (YES) | 1632 (42.46%) | 1800 (43.12%) | 0.56 | 0.014 | 0 |
| Stroke (YES) | **301 (7.83%)** | **261 (6.25%)** | **<0.01** | **0.062** | **0** |
| Malignancy (YES) | **613 (15.95%)** | **791 (18.95%)** | **<0.001** | **0.079** | **0** |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **79.49 (16.97)** | **73.09 (18.04)** | **<0.001** | **0.366** | **0** |
| Temperature | 36.47 (2.90) | 36.54 (1.96) | 0.18 | 0.027 | 0 |
| Heart rate | **90.37 (19.92)** | **88.80 (19.27)** | **<0.01** | **0.08** | **0** |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | 7.36 (0.09) | 7.36 (0.10) | 0.15 | 0.033 | 0 |
| PO2 | **224.32 (127.09)** | **208.33 (126.46)** | **<0.001** | **0.126** | **0** |
| PCO2 | 42.43 (10.33) | 42.27 (10.98) | 0.11 | 0.015 | 0 |
| Lactate | 2.54 (1.86) | 2.63 (2.21) | 0.79 | 0.048 | 0 |
| Creatinine | **1.43 (1.40)** | **1.83 (1.68)** | **<0.001** | **0.256** | **0** |
| WBC | 14.46 (8.72) | 14.45 (9.54) | 0.29 | 0.001 | 0 |
| Hemoglobin | **10.21 (2.23)** | **9.68 (1.98)** | **<0.001** | **0.248** | **0** |
| Platelet | 193.00 (107.90) | 197.53 (115.17) | 0.1 | 0.041 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | **541 (14.07%)** | **1094 (26.21%)** | **<0.001** | **0.306** | **0** |
| ICU mortality (Death) | **342 (8.90%)** | **733 (17.56%)** | **<0.001** | **0.258** | **0** |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | **5.20 (6.37)** | **5.20 (5.77)** | **<0.001** | **<0.001** | **0** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2Low TWA-MAP: TWA-MAP < 70 (mm Hg) | | | | | |

## Supplementary Table 35. Baseline characteristics after propensity score matching of subgroup cohort 1

|  | **Optimal TWA-MAP (N=2834) 1** | **Low TWA-MAP (N=2834) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | **67.63 (13.37)** | **67.98 (14.03)** | **<0.05** | **0.025** | **0** |
| Gender (Female) | 1076 (37.97%) | 1072 (37.83%) | 0.93 | 0.003 | 0 |
| Weight | 83.52 (22.89) | 83.60 (26.21) | 0.76 | 0.003 | 0 |
| SAPS II | 42.87 (13.95) | 42.90 (13.69) | 0.68 | 0.002 | 0 |
| SOFA score | 8.01 (3.80) | 8.00 (3.86) | 0.8 | 0.002 | 0 |
| Charlson comorbidity index | 6.10 (2.66) | 6.12 (2.63) | 0.59 | 0.007 | 0 |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | 1589 (56.07%) | 1619 (57.13%) | 0.44 | 0.021 | 0 |
| Sedative therapy (YES) | 2146 (75.72%) | 2193 (77.38%) | 0.15 | 0.039 | 0 |
| Length of vasopressor therapy | **36.90 (56.10)** | **36.97 (47.10)** | **<0.001** | **0.001** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | 961 (33.91%) | 959 (33.84%) | 0.98 | 0.001 | 0 |
| Hypertension (YES) | 1898 (66.97%) | 1928 (68.03%) | 0.41 | 0.023 | 0 |
| AFIB (YES) | 662 (23.36%) | 675 (23.82%) | 0.71 | 0.011 | 0 |
| Renal (YES) | 683 (24.10%) | 669 (23.61%) | 0.69 | 0.012 | 0 |
| Liver (YES) | 225 (7.94%) | 218 (7.69%) | 0.77 | 0.009 | 0 |
| COPD (YES) | 430 (15.17%) | 420 (14.82%) | 0.74 | 0.01 | 0 |
| CAD (YES) | 1205 (42.52%) | 1257 (44.35%) | 0.17 | 0.037 | 0 |
| Stroke (YES) | 202 (7.13%) | 210 (7.41%) | 0.72 | 0.011 | 0 |
| Malignancy (YES) | 498 (17.57%) | 493 (17.40%) | 0.89 | 0.005 | 0 |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **76.89 (14.94)** | **76.77 (18.64)** | **<0.001** | **0.007** | **0** |
| Temperature | 36.47 (3.02) | 36.52 (1.74) | 0.22 | 0.019 | 0 |
| Heart rate | 90.00 (19.76) | 89.51 (19.17) | 0.56 | 0.025 | 0 |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | 7.36 (0.09) | 7.36 (0.09) | 0.25 | 0.024 | 0 |
| PO2 | 219.29 (127.15) | 220.26 (127.75) | 0.75 | 0.008 | 0 |
| PCO2 | 42.36 (10.72) | 42.24 (10.79) | 0.54 | 0.011 | 0 |
| Lactate | 2.59 (1.96) | 2.59 (2.11) | 0.45 | <0.001 | 0 |
| Creatinine | 1.54 (1.52) | 1.53 (1.44) | 0.93 | 0.01 | 0 |
| WBC | 14.49 (9.08) | 14.47 (9.69) | 0.76 | 0.002 | 0 |
| Hemoglobin | 9.95 (2.16) | 9.88 (2.04) | 0.26 | 0.03 | 0 |
| Platelet | 194.33 (111.92) | 195.02 (110.34) | 0.31 | 0.006 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | **455 (16.06%)** | **601 (21.21%)** | **<0.001** | **0.133** | **0** |
| ICU mortality (Death) | **278 (9.81%)** | **408 (14.40%)** | **<0.001** | **0.141** | **0** |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | 5.33 (6.47) | 4.87 (5.27) | 0.59 | 0.078 | 0 |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2Low TWA-MAP: TWA-MAP < 70 (mm Hg) | | | | | |

## Supplementary Table 36. Standardized mean difference (SMD) of covariates before and after propensity score matching of subgroup cohort 2

| Characteristic | Before matcing | After matcing |
| --- | --- | --- |
| SMD ≤ 0.1 | 17 | 29 |
| SMD > 0.1 | 12 | 0 |
| Total number of covariates | 29 | 29 |

## Supplementary Table 37. Baseline characteristics before propensity score matching of subgroup cohort 2

|  | **Optimal TWA-MAP (N=3844) 1** | **High TWA-MAP (N=1006) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | **65.13 (13.97)** | **61.59 (15.24)** | **<0.001** | **0.242** | **0** |
| Gender (Female) | **1308 (34.03%)** | **409 (40.66%)** | **<0.001** | **0.137** | **0** |
| Weight | **84.25 (22.70)** | **82.75 (23.60)** | **<0.01** | **0.064** | **0** |
| SAPS II | **40.83 (13.90)** | **38.47 (14.13)** | **<0.001** | **0.169** | **0** |
| SOFA score | **7.73 (3.74)** | **7.12 (3.64)** | **<0.001** | **0.166** | **0** |
| Charlson comorbidity index | **5.58 (2.69)** | **5.05 (2.72)** | **<0.001** | **0.195** | **0** |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | 2231 (58.04%) | 581 (57.75%) | 0.9 | 0.006 | 0 |
| Sedative therapy (YES) | 3076 (80.02%) | 823 (81.81%) | 0.22 | 0.046 | 0 |
| Length of vasopressor therapy | **34.11 (51.62)** | **17.76 (34.15)** | **<0.001** | **0.374** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | **1183 (30.78%)** | **262 (26.04%)** | **<0.01** | **0.105** | **0** |
| Hypertension (YES) | **2559 (66.57%)** | **634 (63.02%)** | **<0.05** | **0.074** | **0** |
| AFIB (YES) | 834 (21.70%) | 191 (18.99%) | 0.07 | 0.067 | 0 |
| Renal (YES) | **757 (19.69%)** | **164 (16.30%)** | **<0.05** | **0.088** | **0** |
| Liver (YES) | 236 (6.14%) | 46 (4.57%) | 0.07 | 0.07 | 0 |
| COPD (YES) | **516 (13.42%)** | **103 (10.24%)** | **<0.01** | **0.099** | **0** |
| CAD (YES) | **1632 (42.46%)** | **332 (33.00%)** | **<0.001** | **0.196** | **0** |
| Stroke (YES) | **301 (7.83%)** | **177 (17.59%)** | **<0.001** | **0.296** | **0** |
| Malignancy (YES) | 613 (15.95%) | 148 (14.71%) | 0.36 | 0.034 | 0 |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **79.49 (16.97)** | **88.32 (16.72)** | **<0.001** | **0.525** | **0** |
| Temperature | **36.47 (2.90)** | **36.22 (3.08)** | **<0.01** | **0.085** | **0** |
| Heart rate | **90.37 (19.92)** | **88.72 (20.39)** | **<0.05** | **0.082** | **0** |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | **7.36 (0.09)** | **7.37 (0.09)** | **<0.01** | **0.091** | **0** |
| PO2 | 224.32 (127.09) | 229.74 (126.81) | 0.14 | 0.043 | 0 |
| PCO2 | 42.43 (10.33) | 41.88 (10.72) | 0.06 | 0.052 | 0 |
| Lactate | 2.54 (1.86) | 2.48 (1.84) | 0.36 | 0.03 | 0 |
| Creatinine | **1.43 (1.40)** | **1.32 (1.34)** | **<0.001** | **0.079** | **0** |
| WBC | **14.46 (8.72)** | **13.39 (7.08)** | **<0.001** | **0.134** | **0** |
| Hemoglobin | **10.21 (2.23)** | **10.67 (2.35)** | **<0.001** | **0.202** | **0** |
| Platelet | **193.00 (107.90)** | **195.29 (100.61)** | **<0.05** | **0.022** | **0** |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | 541 (14.07%) | 156 (15.51%) | 0.27 | 0.04 | 0 |
| ICU mortality (Death) | 342 (8.90%) | 100 (9.94%) | 0.34 | 0.036 | 0 |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | **5.20 (6.37)** | **5.24 (6.45)** | **<0.05** | **0.007** | **0** |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2High TWA-MAP: 83 ≤ TWA-MAP (mm Hg) | | | | | |

## Supplementary Table 38. Baseline characteristics after propensity score matching of subgroup cohort 2

|  | **Optimal TWA-MAP (N=967) 1** | **High TWA-MAP (N=967) 2** | **p-value** | **SMD** | **Missing data (%)** |
| --- | --- | --- | --- | --- | --- |
| Age | 61.59 (15.58) | 61.85 (15.16) | 0.65 | 0.017 | 0 |
| Gender (Female) | 360 (37.23%) | 388 (40.12%) | 0.21 | 0.059 | 0 |
| Weight | 82.48 (21.99) | 82.96 (23.68) | 0.82 | 0.021 | 0 |
| SAPS II | 38.11 (13.13) | 38.44 (14.18) | 0.82 | 0.024 | 0 |
| SOFA score | 7.04 (3.56) | 7.15 (3.67) | 0.5 | 0.031 | 0 |
| Charlson comorbidity index | 4.93 (2.77) | 5.05 (2.70) | 0.24 | 0.045 | 0 |
| **Interventions (boolean for 1st 24 h, hours for vasopressor therapy)** |  |  |  |  |  |
| Mechanical ventilation (YES) | 557 (57.60%) | 556 (57.50%) | 1 | 0.002 | 0 |
| Sedative therapy (YES) | 792 (81.90%) | 789 (81.59%) | 0.91 | 0.008 | 0 |
| Length of vasopressor therapy | **19.63 (27.36)** | **17.76 (34.65)** | **<0.001** | **0.06** | **0** |
| **Comorbidities (boolean)** |  |  |  |  |  |
| HF (YES) | 246 (25.44%) | 252 (26.06%) | 0.79 | 0.014 | 0 |
| Hypertension (YES) | 583 (60.29%) | 612 (63.29%) | 0.19 | 0.062 | 0 |
| AFIB (YES) | 186 (19.23%) | 187 (19.34%) | 1 | 0.003 | 0 |
| Renal (YES) | 161 (16.65%) | 161 (16.65%) | 1 | <0.001 | 0 |
| Liver (YES) | 49 (5.07%) | 45 (4.65%) | 0.75 | 0.019 | 0 |
| COPD (YES) | 80 (8.27%) | 100 (10.34%) | 0.14 | 0.071 | 0 |
| CAD (YES) | 323 (33.40%) | 327 (33.82%) | 0.89 | 0.009 | 0 |
| Stroke (YES) | 163 (16.86%) | 146 (15.10%) | 0.32 | 0.048 | 0 |
| Malignancy (YES) | 128 (13.24%) | 144 (14.89%) | 0.33 | 0.048 | 0 |
| **Vital signs (1st 24 h)** |  |  |  |  |  |
| MAP | **86.76 (19.03)** | **87.38 (15.63)** | **<0.001** | **0.036** | **0** |
| Temperature | 36.16 (4.30) | 36.25 (2.93) | 0.07 | 0.024 | 0 |
| Heart rate | 88.92 (19.82) | 88.75 (20.47) | 0.99 | 0.009 | 0 |
| **Laboratory tests (1st 24 h)** |  |  |  |  |  |
| pH | 7.37 (0.09) | 7.37 (0.09) | 0.93 | 0.003 | 0 |
| PO2 | 232.35 (132.14) | 230.95 (127.28) | 0.91 | 0.011 | 0 |
| PCO2 | 41.71 (9.63) | 41.94 (10.29) | 0.88 | 0.024 | 0 |
| Lactate | 2.50 (1.90) | 2.49 (1.86) | 0.86 | 0.003 | 0 |
| Creatinine | 1.30 (1.30) | 1.33 (1.36) | 0.97 | 0.025 | 0 |
| WBC | 13.43 (7.06) | 13.40 (7.15) | 0.86 | 0.004 | 0 |
| Hemoglobin | 10.68 (2.26) | 10.61 (2.33) | 0.53 | 0.028 | 0 |
| Platelet | 193.00 (106.18) | 193.57 (100.56) | 0.3 | 0.006 | 0 |
| **Outcomes (boolean)** |  |  |  |  |  |
| 28-day mortality (Death) | **113 (11.69%)** | **146 (15.10%)** | **<0.05** | **0.1** | **0** |
| ICU mortality (Death) | 72 (7.45%) | 91 (9.41%) | 0.14 | 0.071 | 0 |
| **Length of Stay (days)** |  |  |  |  |  |
| ICU LOS | 4.83 (6.39) | 5.17 (6.43) | 0.67 | 0.053 | 0 |
| Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. Variables in bold have p values < 0.05. | | | | | |
| 1Optimal TWA-MAP: 70 ≤ TWA-MAP < 83 (mm Hg) | | | | | |
| 2High TWA-MAP: 83 ≤ TWA-MAP (mm Hg) | | | | | |

## Supplementary Table 39. Generalized additive model for 28-day mortality of subgroup cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.50 | 1.32, 1.72 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.85 | 0.75, 0.97 | 0.017 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.03 | 1.03, 1.04 | <0.001 |
| SOFA score | 1.23 | 1.20, 1.26 | <0.001 |
| Charlson comorbidity index | 1.12 | 1.09, 1.15 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.53 | 1.33, 1.75 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 40. Piece-wise exponential additive mixed model for 28-day mortality of subgroup cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.62 | 1.45, 1.80 | <0.001 |
| Age | 1.01 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.87 | 0.79, 0.97 | 0.011 |
| Weight | 1.00 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.03 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.21 | 1.19, 1.23 | <0.001 |
| Charlson comorbidity index | 1.09 | 1.06, 1.11 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.44 | 1.30, 1.61 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.071 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 41. Survey-weighted generalised linear model with all covariates using IPW for 28-day mortality of subgroup cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.57 | 1.35, 1.82 | <0.001 |
| Age | 1.02 | 1.02, 1.03 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.93 | 0.79, 1.09 | 0.4 |
| Weight | 1.00 | 0.99, 1.00 | 0.3 |
| SAPS II | 1.03 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.22 | 1.18, 1.25 | <0.001 |
| Charlson comorbidity index | 1.11 | 1.06, 1.15 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.98 | 0.81, 1.20 | 0.9 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.65 | 1.33, 2.04 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.89, 1.23 | 0.6 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.22 | 1.04, 1.43 | 0.014 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.89, 1.24 | 0.6 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.07 | 0.89, 1.30 | 0.5 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.65 | 0.52, 0.83 | <0.001 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.97 | 0.81, 1.16 | 0.7 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.20 | 1.02, 1.40 | 0.026 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.58 | 0.45, 0.76 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.64 | 0.53, 0.77 | <0.001 |
| MAP | 1.00 | 1.00, 1.01 | 0.088 |
| Temperature | 0.98 | 0.96, 1.01 | 0.14 |
| Heart rate | 1.01 | 1.00, 1.01 | <0.001 |
| pH | 0.51 | 0.22, 1.23 | 0.13 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.01 | 0.6 |
| Lactate | 1.06 | 1.03, 1.10 | <0.001 |
| Creatinine | 0.98 | 0.93, 1.03 | 0.4 |
| WBC | 1.00 | 1.00, 1.01 | 0.3 |
| Hemoglobin | 1.01 | 0.97, 1.04 | 0.7 |
| Platelet | 1.00 | 1.00, 1.00 | 0.002 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 42. Proportional hazards assumption for survey-weighted Cox model using IPW for 28-day mortality of subgroup cohort 1

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 1.00 |
| Age | 0.97 |
| Gender | 1.00 |
| Weight | 0.95 |
| SAPS II | 0.95 |
| SOFA score | 0.99 |
| Charlson comorbidity index | 0.96 |
| Mechanical ventilation | 0.98 |
| Sedative therapy | 0.98 |
| Length of vasopressor therapy | 0.89 |
| HF | 0.99 |
| Hypertension | 0.99 |
| AFIB | 0.98 |
| Renal | 0.98 |
| Liver | 0.98 |
| COPD | 1.00 |
| CAD | 0.99 |
| Stroke | 0.98 |
| Malignancy | 0.97 |
| MAP | 1.00 |
| Temperature | 0.99 |
| Heart rate | 0.98 |
| pH | 0.94 |
| PO2 | 0.98 |
| PCO2 | 0.99 |
| Lactate | 0.95 |
| Creatinine | 0.98 |
| WBC | 0.99 |
| Hemoglobin | 0.97 |
| Platelet | 1.00 |
| GLOBAL | 1.00 |

## Supplementary Table 43. Survey-weighted Cox model with all covariates using IPW for 28-day mortality of subgroup cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.64 | 1.45, 1.85 | <0.001 |
| Age | 1.02 | 1.01, 1.03 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.93 | 0.82, 1.05 | 0.2 |
| Weight | 1.00 | 0.99, 1.00 | 0.4 |
| SAPS II | 1.02 | 1.01, 1.02 | <0.001 |
| SOFA score | 1.17 | 1.15, 1.20 | <0.001 |
| Charlson comorbidity index | 1.07 | 1.04, 1.10 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.00 | 0.86, 1.17 | >0.9 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.38 | 1.17, 1.63 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.2 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.03 | 0.91, 1.16 | 0.7 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.18 | 1.04, 1.34 | 0.008 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.07 | 0.94, 1.21 | 0.3 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.91, 1.22 | 0.5 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.78 | 0.66, 0.92 | 0.004 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.96 | 0.84, 1.10 | 0.6 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.16 | 1.02, 1.31 | 0.024 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.73 | 0.60, 0.88 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.72 | 0.62, 0.83 | <0.001 |
| MAP | 1.00 | 1.00, 1.01 | 0.093 |
| Temperature | 0.98 | 0.97, 1.00 | 0.018 |
| Heart rate | 1.01 | 1.00, 1.01 | <0.001 |
| pH | 0.37 | 0.19, 0.73 | 0.004 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.00 | 0.4 |
| Lactate | 1.04 | 1.02, 1.07 | 0.001 |
| Creatinine | 0.99 | 0.96, 1.03 | 0.7 |
| WBC | 1.00 | 1.00, 1.01 | 0.10 |
| Hemoglobin | 1.01 | 0.99, 1.04 | 0.3 |
| Platelet | 1.00 | 1.00, 1.00 | 0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 44. Cox model with all covariates using IPW for 28-day mortality of subgroup cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.62 | 1.45, 1.83 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.93 | 0.83, 1.05 | 0.3 |
| SOFA score | 1.18 | 1.15, 1.20 | <0.001 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.36 | 1.15, 1.61 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.04 | 0.93, 1.17 | 0.5 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.18 | 1.05, 1.33 | 0.007 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.97 | 0.85, 1.10 | 0.6 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.16 | 1.02, 1.31 | 0.019 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.74 | 0.62, 0.88 | <0.001 |
| MAP | 1.00 | 1.00, 1.01 | 0.078 |
| Temperature | 0.98 | 0.97, 0.99 | 0.002 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.00 | 0.5 |
| WBC | 1.00 | 1.00, 1.01 | 0.063 |
| Platelet | 1.00 | 1.00, 1.00 | <0.001 |
| tt(Age) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(Weight) | 1.00 | 1.00, 1.00 | 0.3 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(Charlson comorbidity index) | 1.02 | 1.01, 1.03 | <0.001 |
| tt(Mechanical ventilation) | 1.01 | 0.96, 1.06 | 0.7 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | 0.015 |
| tt(AFIB) | 1.01 | 0.98, 1.05 | 0.5 |
| tt(Renal) | 1.02 | 0.98, 1.06 | 0.4 |
| tt(Liver) | 0.93 | 0.88, 0.97 | 0.003 |
| tt(Malignancy) | 0.90 | 0.87, 0.94 | <0.001 |
| tt(Heart rate) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(pH) | 0.76 | 0.62, 0.93 | 0.008 |
| tt(Lactate) | 1.01 | 1.01, 1.02 | <0.001 |
| tt(Creatinine) | 1.00 | 0.99, 1.01 | 0.6 |
| tt(Hemoglobin) | 1.00 | 1.00, 1.01 | 0.3 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 45. Generalized additive model for 28-day mortality of subgroup cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.58 | 1.27, 1.95 | <0.001 |
| Age | 1.00 | 0.99, 1.01 | 0.6 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.93 | 0.77, 1.12 | 0.4 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.03 | 1.02, 1.04 | <0.001 |
| SOFA score | 1.14 | 1.11, 1.18 | <0.001 |
| Charlson comorbidity index | 1.13 | 1.09, 1.17 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.06 | 0.88, 1.29 | 0.5 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 46. Piece-wise exponential additive mixed model for 28-day mortality of subgroup cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.44 | 1.20, 1.73 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.11 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.94 | 0.80, 1.10 | 0.4 |
| Weight | 0.99 | 0.99, 1.00 | <0.001 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.13 | 1.10, 1.16 | <0.001 |
| Charlson comorbidity index | 1.10 | 1.07, 1.13 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.04 | 0.88, 1.23 | 0.6 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 47. Survey-weighted generalised linear model with all covariates using IPW for 28-day mortality of subgroup cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.80 | 1.36, 2.38 | <0.001 |
| Age | 1.02 | 1.01, 1.03 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 1.01 | 0.81, 1.25 | >0.9 |
| Weight | 0.99 | 0.99, 1.00 | 0.008 |
| SAPS II | 1.02 | 1.01, 1.03 | <0.001 |
| SOFA score | 1.16 | 1.12, 1.21 | <0.001 |
| Charlson comorbidity index | 1.10 | 1.04, 1.16 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.77 | 0.58, 1.01 | 0.059 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 2.22 | 1.62, 3.03 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.09 | 0.87, 1.38 | 0.5 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.42 | 1.14, 1.76 | 0.002 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.10 | 0.85, 1.41 | 0.5 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.03 | 0.76, 1.41 | 0.8 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.59, 1.22 | 0.4 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.81 | 0.63, 1.05 | 0.12 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.40 | 1.11, 1.78 | 0.005 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.37 | 0.27, 0.49 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.76 | 0.59, 0.99 | 0.041 |
| MAP | 1.00 | 1.00, 1.01 | 0.4 |
| Temperature | 0.98 | 0.96, 1.01 | 0.13 |
| Heart rate | 1.01 | 1.00, 1.01 | 0.027 |
| pH | 1.89 | 0.54, 6.64 | 0.3 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.01 | 0.7 |
| Lactate | 1.09 | 1.03, 1.14 | <0.001 |
| Creatinine | 0.98 | 0.90, 1.06 | 0.6 |
| WBC | 1.01 | 1.00, 1.02 | 0.043 |
| Hemoglobin | 1.03 | 0.98, 1.08 | 0.2 |
| Platelet | 1.00 | 1.00, 1.00 | 0.003 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 48. Proportional hazards assumption for survey-weighted Cox model using IPW for 28-day mortality of subgroup cohort 2

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 0.96 |
| Age | 0.93 |
| Gender | 0.99 |
| Weight | 0.97 |
| SAPS II | 0.96 |
| SOFA score | 1.00 |
| Charlson comorbidity index | 0.94 |
| Mechanical ventilation | 0.97 |
| Sedative therapy | 0.99 |
| Length of vasopressor therapy | 0.94 |
| HF | 0.97 |
| Hypertension | 0.98 |
| AFIB | 0.99 |
| Renal | 0.96 |
| Liver | 0.95 |
| COPD | 0.97 |
| CAD | 1.00 |
| Stroke | 0.99 |
| Malignancy | 0.98 |
| MAP | 0.99 |
| Temperature | 1.00 |
| Heart rate | 0.99 |
| pH | 0.97 |
| PO2 | 1.00 |
| PCO2 | 1.00 |
| Lactate | 0.95 |
| Creatinine | 0.99 |
| WBC | 0.99 |
| Hemoglobin | 0.95 |
| Platelet | 1.00 |
| GLOBAL | 1.00 |

## Supplementary Table 49. Survey-weighted Cox model with all covariates using IPW for 28-day mortality of subgroup cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.64 | 1.31, 2.07 | <0.001 |
| Age | 1.02 | 1.01, 1.03 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 1.02 | 0.85, 1.22 | 0.8 |
| Weight | 0.99 | 0.99, 1.00 | 0.024 |
| SAPS II | 1.02 | 1.01, 1.03 | <0.001 |
| SOFA score | 1.13 | 1.09, 1.17 | <0.001 |
| Charlson comorbidity index | 1.08 | 1.03, 1.13 | <0.001 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.78 | 0.61, 1.00 | 0.049 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 2.03 | 1.53, 2.69 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.013 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.08 | 0.89, 1.30 | 0.4 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.37 | 1.14, 1.65 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.09 | 0.88, 1.35 | 0.4 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.11 | 0.86, 1.42 | 0.4 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.89 | 0.67, 1.18 | 0.4 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.69, 1.05 | 0.14 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.28 | 1.05, 1.57 | 0.015 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.46 | 0.36, 0.58 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.79 | 0.64, 0.99 | 0.037 |
| MAP | 1.00 | 1.00, 1.01 | 0.8 |
| Temperature | 0.98 | 0.97, 1.00 | 0.079 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.017 |
| pH | 1.59 | 0.53, 4.81 | 0.4 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.3 |
| Lactate | 1.06 | 1.02, 1.10 | 0.002 |
| Creatinine | 0.99 | 0.93, 1.06 | 0.8 |
| WBC | 1.01 | 1.00, 1.02 | 0.033 |
| Hemoglobin | 1.04 | 1.00, 1.08 | 0.042 |
| Platelet | 1.00 | 1.00, 1.00 | 0.006 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 50. Cox model with all covariates using IPW for 28-day mortality of subgroup cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 1.02 | 0.86, 1.22 | 0.8 |
| SOFA score | 1.14 | 1.10, 1.17 | <0.001 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.98 | 1.50, 2.63 | <0.001 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.38 | 1.16, 1.65 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.08 | 0.88, 1.34 | 0.5 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.29 | 1.06, 1.57 | 0.012 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.45 | 0.36, 0.56 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.79 | 0.65, 0.97 | 0.022 |
| MAP | 1.00 | 1.00, 1.00 | 0.8 |
| Temperature | 0.98 | 0.97, 1.00 | 0.054 |
| Heart rate | 1.01 | 1.00, 1.01 | 0.013 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 1.00, 1.01 | 0.3 |
| Creatinine | 0.99 | 0.93, 1.05 | 0.7 |
| WBC | 1.01 | 1.00, 1.02 | 0.031 |
| Platelet | 1.00 | 1.00, 1.00 | 0.004 |
| tt(Group) | 1.16 | 1.09, 1.23 | <0.001 |
| tt(Age) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(Weight) | 1.00 | 1.00, 1.00 | 0.021 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(Charlson comorbidity index) | 1.02 | 1.01, 1.04 | <0.001 |
| tt(Mechanical ventilation) | 0.94 | 0.87, 1.01 | 0.075 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | 0.002 |
| tt(HF) | 1.02 | 0.97, 1.08 | 0.4 |
| tt(Renal) | 1.03 | 0.96, 1.10 | 0.5 |
| tt(Liver) | 0.96 | 0.87, 1.04 | 0.3 |
| tt(COPD) | 0.95 | 0.89, 1.01 | 0.11 |
| tt(pH) | 1.15 | 0.84, 1.59 | 0.4 |
| tt(Lactate) | 1.02 | 1.01, 1.03 | <0.001 |
| tt(Hemoglobin) | 1.01 | 1.00, 1.02 | 0.054 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 51. Generalized additive model for ICU mortality of subgroup cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.60 | 1.36, 1.87 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.051 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.81 | 0.69, 0.95 | 0.008 |
| Weight | 1.00 | 0.99, 1.00 | 0.042 |
| SAPS II | 1.04 | 1.03, 1.04 | <0.001 |
| SOFA score | 1.24 | 1.21, 1.28 | <0.001 |
| Charlson comorbidity index | 1.05 | 1.01, 1.08 | 0.004 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.08 | 0.91, 1.26 | 0.4 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 52. Piece-wise exponential additive mixed model for ICU mortality of subgroup cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.71 | 1.50, 1.96 | <0.001 |
| Age | 1.01 | 1.00, 1.01 | 0.012 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.91 | 0.80, 1.03 | 0.13 |
| Weight | 1.00 | 0.99, 1.00 | 0.037 |
| SAPS II | 1.03 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.16 | 1.13, 1.18 | <0.001 |
| Charlson comorbidity index | 1.03 | 1.01, 1.06 | 0.009 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.44 | 1.26, 1.65 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 53. Survey-weighted generalised linear model with all covariates using IPW for ICU mortality of subgroup cohort 1

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.83 | 1.53, 2.19 | <0.001 |
| Age | 1.02 | 1.01, 1.03 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.90 | 0.76, 1.07 | 0.2 |
| Weight | 1.00 | 0.99, 1.00 | 0.2 |
| SAPS II | 1.03 | 1.02, 1.04 | <0.001 |
| SOFA score | 1.23 | 1.18, 1.27 | <0.001 |
| Charlson comorbidity index | 1.06 | 1.01, 1.10 | 0.022 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.82 | 0.64, 1.03 | 0.093 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.45 | 1.11, 1.89 | 0.006 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.01 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 0.99 | 0.82, 1.19 | 0.9 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.16 | 0.96, 1.39 | 0.12 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.21 | 0.98, 1.48 | 0.072 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.10 | 0.88, 1.39 | 0.4 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.68, 1.19 | 0.5 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.89 | 0.72, 1.10 | 0.3 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.07 | 0.89, 1.29 | 0.5 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.53 | 0.39, 0.71 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.79 | 0.64, 0.98 | 0.033 |
| MAP | 1.00 | 1.00, 1.01 | 0.051 |
| Temperature | 0.98 | 0.95, 1.00 | 0.052 |
| Heart rate | 1.01 | 1.01, 1.01 | <0.001 |
| pH | 0.21 | 0.08, 0.55 | 0.002 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.00 | 0.3 |
| Lactate | 1.09 | 1.05, 1.13 | <0.001 |
| Creatinine | 0.95 | 0.90, 1.00 | 0.064 |
| WBC | 1.00 | 0.99, 1.01 | 0.7 |
| Hemoglobin | 1.04 | 1.00, 1.08 | 0.082 |
| Platelet | 1.00 | 1.00, 1.00 | 0.035 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 54. Proportional hazards assumption for survey-weighted Cox model using IPW for ICU mortality of subgroup cohort 1

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 0.99 |
| Age | 0.98 |
| Gender | 0.99 |
| Weight | 0.98 |
| SAPS II | 0.93 |
| SOFA score | 0.96 |
| Charlson comorbidity index | 0.99 |
| Mechanical ventilation | 0.95 |
| Sedative therapy | 0.97 |
| Length of vasopressor therapy | 0.91 |
| HF | 0.98 |
| Hypertension | 0.99 |
| AFIB | 1.00 |
| Renal | 0.99 |
| Liver | 0.98 |
| COPD | 1.00 |
| CAD | 0.99 |
| Stroke | 1.00 |
| Malignancy | 1.00 |
| MAP | 0.99 |
| Temperature | 0.99 |
| Heart rate | 0.96 |
| pH | 0.95 |
| PO2 | 0.98 |
| PCO2 | 1.00 |
| Lactate | 0.96 |
| Creatinine | 0.98 |
| WBC | 1.00 |
| Hemoglobin | 0.98 |
| Platelet | 0.99 |
| GLOBAL | 1.00 |

## Supplementary Table 55. Survey-weighted Cox model with all covariates using IPW for ICU mortality of subgroup cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.84 | 1.57, 2.16 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.94 | 0.82, 1.09 | 0.4 |
| Weight | 1.00 | 1.00, 1.00 | 0.4 |
| SAPS II | 1.02 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.11 | 1.08, 1.14 | <0.001 |
| Charlson comorbidity index | 1.04 | 1.00, 1.08 | 0.062 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.07 | 0.88, 1.30 | 0.5 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.44 | 1.16, 1.79 | 0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 0.99 | 0.85, 1.16 | >0.9 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.21 | 1.04, 1.42 | 0.013 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.37 | 1.16, 1.63 | <0.001 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.11 | 0.92, 1.33 | 0.3 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.70, 1.05 | 0.13 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.99 | 0.83, 1.18 | >0.9 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.95 | 0.81, 1.11 | 0.5 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.91 | 0.72, 1.14 | 0.4 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.86 | 0.71, 1.04 | 0.11 |
| MAP | 1.00 | 1.00, 1.01 | 0.3 |
| Temperature | 0.97 | 0.95, 1.00 | 0.027 |
| Heart rate | 1.01 | 1.00, 1.01 | <0.001 |
| pH | 0.20 | 0.09, 0.45 | <0.001 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.00 | 0.13 |
| Lactate | 1.05 | 1.03, 1.08 | <0.001 |
| Creatinine | 1.03 | 0.98, 1.07 | 0.2 |
| WBC | 1.00 | 1.00, 1.01 | 0.3 |
| Hemoglobin | 1.02 | 0.99, 1.06 | 0.2 |
| Platelet | 1.00 | 1.00, 1.00 | 0.7 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 56. Cox model with all covariates using IPW for ICU mortality of subgroup cohort 1

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| TWA-MAP < 70 (mm Hg) | 1.83 | 1.58, 2.13 | <0.001 |
| Age | 1.02 | 1.01, 1.02 | <0.001 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.94 | 0.82, 1.08 | 0.4 |
| Weight | 1.00 | 1.00, 1.00 | 0.4 |
| Charlson comorbidity index | 1.04 | 1.00, 1.07 | 0.037 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.00 | 0.87, 1.16 | >0.9 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.21 | 1.04, 1.41 | 0.012 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.38 | 1.17, 1.62 | <0.001 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.11 | 0.93, 1.33 | 0.2 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.69, 1.04 | 0.12 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.99 | 0.84, 1.16 | 0.9 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.96 | 0.83, 1.12 | 0.6 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.90 | 0.73, 1.12 | 0.4 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.85 | 0.72, 1.01 | 0.063 |
| MAP | 1.00 | 1.00, 1.01 | 0.3 |
| Temperature | 0.97 | 0.96, 0.99 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.00 | 0.12 |
| Creatinine | 1.03 | 0.99, 1.07 | 0.2 |
| WBC | 1.00 | 1.00, 1.01 | 0.2 |
| Platelet | 1.00 | 1.00, 1.00 | 0.7 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(SOFA score) | 1.03 | 1.03, 1.04 | <0.001 |
| tt(Mechanical ventilation) | 1.03 | 0.97, 1.09 | 0.4 |
| tt(Sedative therapy) | 1.12 | 1.04, 1.19 | 0.002 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(Heart rate) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(pH) | 0.62 | 0.49, 0.78 | <0.001 |
| tt(PO2) | 1.00 | 1.00, 1.00 | <0.001 |
| tt(Lactate) | 1.02 | 1.01, 1.02 | <0.001 |
| tt(Hemoglobin) | 1.01 | 1.00, 1.02 | 0.2 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 57. Generalized additive model for ICU mortality of subgroup cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.65 | 1.27, 2.14 | <0.001 |
| Age | 1.00 | 0.99, 1.01 | 0.8 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.85 | 0.68, 1.06 | 0.2 |
| Weight | 0.99 | 0.99, 1.00 | 0.009 |
| SAPS II | 1.04 | 1.03, 1.05 | <0.001 |
| SOFA score | 1.12 | 1.08, 1.16 | <0.001 |
| Charlson comorbidity index | 1.04 | 1.00, 1.09 | 0.058 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.78 | 0.62, 1.00 | 0.050 |
| Length of vasopressor therapy | 1.01 | 1.01, 1.01 | <0.001 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 58. Piece-wise exponential additive mixed model for ICU mortality of subgroup cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.32 | 1.04, 1.66 | 0.021 |
| Age | 1.00 | 1.00, 1.01 | 0.3 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.91 | 0.74, 1.11 | 0.3 |
| Weight | 0.99 | 0.99, 1.00 | 0.030 |
| SAPS II | 1.03 | 1.02, 1.04 | <0.001 |
| SOFA score | 1.07 | 1.04, 1.10 | <0.001 |
| Charlson comorbidity index | 1.03 | 0.99, 1.07 | 0.13 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 1.09 | 0.87, 1.36 | 0.4 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.11 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 59. Survey-weighted generalised linear model with all covariates using IPW for ICU mortality of subgroup cohort 2

| Characteristic | OR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.67 | 1.19, 2.35 | 0.003 |
| Age | 1.02 | 1.00, 1.03 | 0.014 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.88 | 0.67, 1.15 | 0.4 |
| Weight | 1.00 | 0.99, 1.00 | 0.11 |
| SAPS II | 1.03 | 1.02, 1.04 | <0.001 |
| SOFA score | 1.14 | 1.08, 1.20 | <0.001 |
| Charlson comorbidity index | 1.05 | 0.98, 1.13 | 0.14 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.66 | 0.46, 0.96 | 0.029 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 1.76 | 1.15, 2.68 | 0.009 |
| Length of vasopressor therapy | 1.01 | 1.00, 1.01 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.10 | 0.83, 1.46 | 0.5 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.55 | 1.19, 2.01 | 0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.16 | 0.85, 1.58 | 0.4 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.35 | 0.91, 1.99 | 0.13 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 1.05 | 0.68, 1.61 | 0.8 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.79 | 0.58, 1.08 | 0.14 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 1.22 | 0.91, 1.64 | 0.2 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.32 | 0.23, 0.45 | <0.001 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.87 | 0.64, 1.20 | 0.4 |
| MAP | 1.00 | 1.00, 1.01 | 0.5 |
| Temperature | 0.97 | 0.94, 0.99 | 0.014 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.11 |
| pH | 2.59 | 0.61, 11.0 | 0.2 |
| PO2 | 1.00 | 1.00, 1.00 | <0.001 |
| PCO2 | 1.00 | 0.99, 1.02 | 0.4 |
| Lactate | 1.10 | 1.04, 1.16 | 0.001 |
| Creatinine | 1.00 | 0.91, 1.10 | >0.9 |
| WBC | 1.01 | 1.00, 1.02 | 0.3 |
| Hemoglobin | 1.07 | 1.01, 1.13 | 0.021 |
| Platelet | 1.00 | 1.00, 1.00 | 0.036 |
| 1OR = Odds Ratio, CI = Confidence Interval | | | |

## Supplementary Table 60. Proportional hazards assumption for survey-weighted Cox model using IPW for ICU mortality of subgroup cohort 2

| Covariate | p-value of PH assumption |
| --- | --- |
| Group | 0.95 |
| Age | 0.96 |
| Gender | 0.97 |
| Weight | 0.98 |
| SAPS II | 0.95 |
| SOFA score | 0.98 |
| Charlson comorbidity index | 0.97 |
| Mechanical ventilation | 0.96 |
| Sedative therapy | 0.98 |
| Length of vasopressor therapy | 0.95 |
| HF | 0.98 |
| Hypertension | 1.00 |
| AFIB | 0.99 |
| Renal | 0.99 |
| Liver | 0.94 |
| COPD | 0.97 |
| CAD | 0.99 |
| Stroke | 0.97 |
| Malignancy | 0.99 |
| MAP | 0.97 |
| Temperature | 0.99 |
| Heart rate | 0.99 |
| pH | 0.96 |
| PO2 | 0.99 |
| PCO2 | 0.99 |
| Lactate | 0.95 |
| Creatinine | 0.98 |
| WBC | 0.99 |
| Hemoglobin | 0.96 |
| Platelet | 1.00 |
| GLOBAL | 1.00 |

## Supplementary Table 61. Survey-weighted Cox model with all covariates using IPW for ICU mortality of subgroup cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Group |  |  |  |
| 70 ≤ TWA-MAP < 83 (mm Hg) | — | — |  |
| 83 ≤ TWA-MAP (mm Hg) | 1.55 | 1.13, 2.11 | 0.006 |
| Age | 1.01 | 1.00, 1.03 | 0.006 |
| Gender |  |  |  |
| Female | — | — |  |
| Male | 0.92 | 0.73, 1.16 | 0.5 |
| Weight | 1.00 | 0.99, 1.00 | 0.3 |
| SAPS II | 1.03 | 1.02, 1.03 | <0.001 |
| SOFA score | 1.06 | 1.02, 1.10 | 0.003 |
| Charlson comorbidity index | 1.05 | 0.99, 1.11 | 0.13 |
| Mechanical ventilation |  |  |  |
| YES | — | — |  |
| NO | 0.83 | 0.60, 1.16 | 0.3 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 2.22 | 1.53, 3.24 | <0.001 |
| Length of vasopressor therapy | 1.00 | 1.00, 1.00 | 0.066 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.10 | 0.86, 1.39 | 0.4 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.53 | 1.23, 1.92 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.17 | 0.89, 1.53 | 0.2 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.45 | 1.04, 2.03 | 0.031 |
| Liver |  |  |  |
| YES | — | — |  |
| NO | 0.91 | 0.65, 1.30 | 0.6 |
| COPD |  |  |  |
| YES | — | — |  |
| NO | 0.89 | 0.68, 1.15 | 0.4 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.93 | 0.72, 1.19 | 0.6 |
| Stroke |  |  |  |
| YES | — | — |  |
| NO | 0.67 | 0.50, 0.91 | 0.010 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.83 | 0.63, 1.10 | 0.2 |
| MAP | 1.00 | 0.99, 1.00 | 0.5 |
| Temperature | 0.97 | 0.95, 0.99 | 0.002 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.3 |
| pH | 2.91 | 0.75, 11.2 | 0.12 |
| PO2 | 1.00 | 1.00, 1.00 | 0.033 |
| PCO2 | 1.00 | 0.99, 1.01 | 0.8 |
| Lactate | 1.08 | 1.03, 1.13 | <0.001 |
| Creatinine | 1.06 | 0.98, 1.15 | 0.15 |
| WBC | 1.01 | 1.00, 1.02 | 0.009 |
| Hemoglobin | 1.06 | 1.02, 1.11 | 0.010 |
| Platelet | 1.00 | 1.00, 1.00 | 0.6 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |

## Supplementary Table 62. Cox model with all covariates using IPW for ICU mortality of subgroup cohort 2

| Characteristic | HR1 | 95% CI1 | p-value |
| --- | --- | --- | --- |
| Weight | 1.00 | 0.99, 1.00 | 0.3 |
| SOFA score | 1.07 | 1.02, 1.11 | 0.002 |
| Sedative therapy |  |  |  |
| YES | — | — |  |
| NO | 2.16 | 1.47, 3.19 | <0.001 |
| HF |  |  |  |
| YES | — | — |  |
| NO | 1.11 | 0.88, 1.39 | 0.4 |
| Hypertension |  |  |  |
| YES | — | — |  |
| NO | 1.54 | 1.23, 1.91 | <0.001 |
| AFIB |  |  |  |
| YES | — | — |  |
| NO | 1.17 | 0.89, 1.55 | 0.3 |
| Renal |  |  |  |
| YES | — | — |  |
| NO | 1.46 | 1.07, 2.00 | 0.018 |
| CAD |  |  |  |
| YES | — | — |  |
| NO | 0.92 | 0.72, 1.18 | 0.5 |
| Malignancy |  |  |  |
| YES | — | — |  |
| NO | 0.83 | 0.65, 1.06 | 0.13 |
| Temperature | 0.97 | 0.95, 0.99 | 0.003 |
| Heart rate | 1.00 | 1.00, 1.01 | 0.2 |
| PO2 | 1.00 | 1.00, 1.00 | 0.035 |
| PCO2 | 1.00 | 0.99, 1.01 | 0.7 |
| Creatinine | 1.06 | 0.98, 1.15 | 0.12 |
| WBC | 1.01 | 1.00, 1.02 | 0.008 |
| Platelet | 1.00 | 1.00, 1.00 | 0.5 |
| tt(Group) | 1.14 | 1.05, 1.25 | 0.003 |
| tt(Age) | 1.00 | 1.00, 1.01 | 0.002 |
| tt(Gender) | 0.97 | 0.90, 1.04 | 0.4 |
| tt(SAPS II) | 1.01 | 1.00, 1.01 | <0.001 |
| tt(Charlson comorbidity index) | 1.01 | 1.00, 1.03 | 0.083 |
| tt(Mechanical ventilation) | 0.95 | 0.86, 1.06 | 0.3 |
| tt(Length of vasopressor therapy) | 1.00 | 1.00, 1.00 | 0.14 |
| tt(Liver) | 0.96 | 0.86, 1.08 | 0.5 |
| tt(COPD) | 0.96 | 0.89, 1.04 | 0.3 |
| tt(Stroke) | 0.89 | 0.82, 0.97 | 0.009 |
| tt(MAP) | 1.00 | 1.00, 1.00 | 0.4 |
| tt(pH) | 1.41 | 0.94, 2.10 | 0.093 |
| tt(Lactate) | 1.02 | 1.01, 1.03 | <0.001 |
| tt(Hemoglobin) | 1.02 | 1.00, 1.03 | 0.009 |
| 1HR = Hazard Ratio, CI = Confidence Interval | | | |