### Supplemental Table 1. Additional Multivariate Models Containing CCL2

| Variable                     | Unit Odds Ratio | 95% Confidence Interval | P value |
|------------------------------|-----------------|--------------------------|---------|
| **Multivariate Analysis by APACHE IV and Initial ICU MAP (ROC AUC: 0.82)** |                 |                          |         |
| APACHE IV                    | 2.8             | 1.7 – 4.8                | <0.0001*|
| CCL2                         | 2.4             | 1.4 – 4.2                | 0.0002* |
| Initial ICU MAP              | 1.7             | 1.1 – 2.8                | 0.02    |
| Total Opioid                 | 1.2             | 0.8 – 1.8                | 0.31    |
| **Multivariate Analysis by APACHE IV and Lowest MAP (ROC AUC: 0.79)** |                 |                          |         |
| APACHE IV                    | 2.6             | 1.6 – 4.5                | 0.0001* |
| CCL2                         | 2.4             | 1.4 – 4.0                | 0.0004* |
| Total Opioid                 | 1.4             | 0.9 – 2.0                | 0.1     |
| Lowest MAP                   | 1.4             | 0.8 – 2.2                | 0.2     |
| **Multivariate Analysis by APACHE IV and Shock (ROC AUC: 0.78)**     |                 |                          |         |
| APACHE IV                    | 2.4             | 1.4 – 4.2                | 0.0004* |
| CCL2                         | 2.3             | 1.4 – 3.8                | 0.0005* |
| Total Opioid                 | 1.3             | 0.9 – 1.8                | 0.24    |
| Shock                        | 1.0             | 0.6 – 1.6                | 0.87    |
| **Multivariate Analysis by APACHE IV and Sepsis (ROC AUC: 0.79)**     |                 |                          |         |
| APACHE IV                    | 2.3             | 1.4 – 3.8                | 0.0002* |
| CCL2                         | 2.2             | 1.3 – 3.8                | 0.002   |
| Total Opioid                 | 1.2             | 0.8 – 1.8                | 0.28    |
| Sepsis                       | 1.1             | 0.7 – 1.8                | 0.64    |

*p ≤ 0.05. Variables standardized. APACHE IV: Acute Physiology and Chronic Health Evaluation Score; CCL2: C-C motif ligand 2; MAP: Mean Arterial Pressure; and ROC AUC: receiving operator characteristic area under curve.
Supplemental Table 2. Additional Multivariate Models Containing Midazolam

| Variable                             | Unit Odds Ratio | 95% Confidence Interval | P value  |
|--------------------------------------|-----------------|--------------------------|----------|
| **Multivariate Analysis by SOFA and Initial ICU MAP (ROC AUC: 0.84)** |                 |                          |          |
| SOFA                                 | 3.5             | 1.6 – 7.5                | 0.0002*  |
| CCL2                                 | 2.9             | 1.4 – 5.9                | 0.001*   |
| Initial ICU MAP                      | 2.2             | 1.1 – 4.4                | 0.02*    |
| Total Midazolam                      | 1.0             | 0.6 – 1.7                | 0.86     |
| Age                                  | 0.6             | 0.3 – 1.0                | 0.05*    |
| **Multivariate Analysis by SOFA and Lowest MAP (ROC AUC: 0.81)** |                 |                          |          |
| CCL2                                 | 2.9             | 1.4 – 6.1                | 0.001*   |
| SOFA                                 | 2.9             | 1.4 – 5.9                | 0.002*   |
| Lowest MAP                           | 1.6             | 0.6 – 3.8                | 0.32     |
| Total Midazolam                      | 1.3             | 0.7 – 2.4                | 0.35     |
| Age                                  | 0.6             | 0.3 – 1.0                | 0.04*    |
| **Multivariate Analysis by SOFA and Shock (ROC AUC: 0.83)** |                 |                          |          |
| CCL2                                 | 2.8             | 1.4 – 5.7                | 0.001*   |
| SOFA                                 | 2.5             | 1.2 – 4.9                | 0.005*   |
| Total Midazolam                      | 1.2             | 0.7 – 1.9                | 0.58     |
| Shock                                | 1.0             | 0.6 – 1.8                | 0.99     |
| Age                                  | 0.5             | 0.3 – 1.0                | 0.04*    |
| **Multivariate Analysis by SOFA and Sepsis (ROC AUC: 0.85)** |                 |                          |          |
| SOFA                                 | 2.4             | 1.3 – 4.7                | 0.004*   |
| CCL2                                 | 2.4             | 1.1 – 4.9                | 0.01*    |
| Sepsis                               | 1.8             | 1.0 – 3.1                | 0.05*    |
| Total Midazolam                      | 1.0             | 0.6 – 1.7                | 1.0      |
| Age                                  | 0.6             | 0.3 – 1.0                | 0.04*    |

*p ⩽ 0.05. Variables standardized. CCL2: C-C motif ligand 2; MAP: Mean Arterial Pressure; ROC AUC: receiving operator characteristic area under curve; and SOFA: Sequential Organ Failure Assessment.
Supplemental Table 3. Additional Multivariate Models Containing Propofol

| Variable                | Unit Odds Ratio | 95% Confidence Interval | P value   |
|-------------------------|-----------------|--------------------------|-----------|
| **Multivariate Analysis by SOFA and Initial ICU MAP (ROC AUC: 0.89)** |                |                          |           |
| CCL2                    | 4.6             | 1.7 – 12.5               | 0.0004*   |
| SOFA                    | 3.2             | 1.1 – 9.1                | 0.01*     |
| Initial ICU MAP         | 1.8             | 0.8 – 3.9                | 0.12      |
| Total Propofol          | 1.3             | 0.4 – 4.5                | 0.56      |
| Age                     | 0.4             | 0.1 – 1.0                | 0.03*     |
| **Multivariate Analysis by SOFA and Lowest MAP (ROC AUC: 0.90)**     |                |                          |           |
| CCL2                    | 5.1             | 1.6 – 15.9               | 0.0003*   |
| SOFA                    | 3.2             | 0.2 – 0.9                | 0.01*     |
| Lowest MAP              | 1.7             | 0.8 – 3.4                | 0.14      |
| Total Propofol          | 1.6             | 0.4 – 6.7                | 0.36      |
| Age                     | 0.4             | 0.2 – 0.9                | 0.02*     |
| **Multivariate Analysis by SOFA and Shock (ROC AUC: 0.90)**           |                |                          |           |
| CCL2                    | 7.3             | 2.0 – 27.2               | 0.0001*   |
| SOFA                    | 3.4             | 1.2 – 9.6                | 0.005*    |
| Total Propofol          | 1.7             | 0.5 – 5.5                | 0.21      |
| Shock                   | 0.3             | 0.1 – 1.1                | 0.03*     |
| Age                     | 0.3             | 0.1 – 0.8                | 0.007*    |
| **Multivariate Analysis by SOFA and Sepsis (ROC AUC: 0.87)**          |                |                          |           |
| CCL2                    | 5.1             | 1.5 – 17.2               | 0.001*    |
| SOFA                    | 2.4             | 1.0 – 6.1                | 0.03*     |
| Total Propofol          | 1.6             | 0.3 – 8.2                | 0.43      |
| Sepsis                  | 0.8             | 0.3 – 1.9                | 0.58      |
| Age                     | 0.4             | 0.1 – 0.9                | 0.01*     |

*p ≤ 0.05. Variables standardized. CCL2: C-C motif ligand 2; MAP: Mean Arterial Pressure; ROC AUC: receiving operator characteristic area under curve; and SOFA: Sequential Organ Failure Assessment.
## Supplemental Table 4. Additional Multivariate Models Containing Dexmedetomidine

| Variable                  | Unit Odds Ratio | 95% Confidence Interval | P value   |
|---------------------------|-----------------|-------------------------|-----------|
| **Multivariate Analysis by SOFA and Initial ICU MAP (ROC AUC: 0.89)** |                 |                         |           |
| CCL2                      | 8.1             | 2.1 – 31.5              | <0.0001*  |
| SOFA                      | 3.0             | 1.0 – 9.0               | 0.03*     |
| Initial ICU MAP           | 1.0             | 0.9 – 1.1               | 0.79      |
| Total Dexmedetomidine     | 1.0             | 0.6 – 1.9               | 0.90      |
| Age                       | 0.1             | 0.0 – 0.5               | 0.0004*   |
| **Multivariate Analysis by SOFA and Lowest MAP (ROC AUC: 0.89)** |                 |                         |           |
| CCL2                      | 7.9             | 2.2 – 28.7              | 0.001*    |
| SOFA                      | 3.4             | 1.0 – 11.5              | 0.03*     |
| Lowest MAP                | 1.1             | 0.4 – 3.2               | 0.84      |
| Total Dexmedetomidine     | 1.0             | 0.5 – 2.0               | 0.89      |
| Age                       | 0.2             | 0.05 – 0.5              | 0.001*    |
| **Multivariate Analysis by SOFA and Shock (ROC AUC: 0.90)** |                 |                         |           |
| CCL2                      | 7.8             | 2.2 – 28.0              | <0.0001*  |
| SOFA                      | 2.9             | 0.9 – 8.7               | 0.05*     |
| Total Dexmedetomidine     | 1.0             | 0.6 – 1.9               | 0.94      |
| Shock                     | 1.3             | 0.5 – 3.3               | 0.57      |
| Age                       | 0.2             | 0.1 – 0.5               | 0.0002*   |
| **Multivariate Analysis by SOFA and Sepsis (ROC AUC: 0.90)** |                 |                         |           |
| CCL2                      | 7.0             | 1.9 – 26.2              | 0.0002*   |
| SOFA                      | 3.2             | 1.1 – 9.5               | 0.02*     |
| Sepsis                    | 1.2             | 0.5 – 2.7               | 0.68      |
| Total Dexmedetomidine     | 1.0             | 0.5 – 1.9               | 0.98      |
| Age                       | 0.2             | 0.1 – 0.5               | 0.0002*   |

*p ≤ 0.05. Variables standardized. CCL2: C-C motif ligand 2; MAP: Mean Arterial Pressure; ROC AUC: receiving operator characteristic area under curve; and SOFA: Sequential Organ Failure Assessment.