

**S2 Table. Demographic and clinical characteristics before and after propensity weighting of all enrolled patients in the United States.**

| Clinical Characteristic                   | Patient Characteristics before Propensity Weighting |   |         | Patient Characteristics after Propensity Weighting     |  |         |
|---|---|---|---------|--|--|---------|
|   | No Respiratory Depression Episode (n=272)           | ≥1 Respiratory Depression Episode (n=148) | p-value | No Respiratory Depression Episode (n=255) <sup>a</sup> | ≥1 Respiratory Depression Episode (n=128) <sup>a</sup> | p-value |
| <b>Age (yr) (Mean ± SD)</b>               | 52.4 ± 14.1   | 62.4 ± 11.5                               |         | 55.4 ± 14.1  | 58.1 ± 11.2  |         |
| <60                                       | 67.6% (184/272)                                     | 38.5% (57/148)                            | <.0001  | 57.7% (147/255)  | 56.9% (73/128)   | .996    |
| ≥60 - <70                                 | 20.6% (56/272)                                      | 34.5% (51/148)                            |         | 25.8% (66/255)   | 25.8% (33/128)   |         |
| ≥70 - <80                                 | 9.9% (27/272)                                       | 20.9% (31/148)                            |         | 13.3% (34/255)   | 13.7% (18/128)   |         |
| ≥80                                       | 1.8% (5/272)  | 6.1% (9/148)                              |         | 3.2% (8/255)   | 3.6% (5/128)   |         |
| <b>Sex (Male)</b>                         | 30.9% (84/272)                                      | 50.7% (75/148)                            | <.0001  | 36.7% (94/255)   | 44.5% (57/128)   | .141    |
| <b>BMI (kg/m<sup>2</sup>) (Mean ± SD)</b> | 32.4 ± 9.6  | 30.2 ± 6.1                                |         |  |  |         |
| <20                                       | 3.7% (10/272)                                       | 2% (3/148)                                | .023    | 1.9% (5/255)   | 1.1% (1/128)   | .748    |
| ≥20 - <25                                 | 16.9% (46/272)                                      | 16.9% (25/148)                            |         | 18% (46/255)   | 19.8% (25/128)   |         |
| ≥25 - <30                                 | 27.6% (75/272)                                      | 35.1% (52/148)                            |         | 30.4% (77/255)   | 27.8% (36/128)   |         |
| ≥30 - <35                                 | 19.5% (53/272)                                      | 27% (40/148)                              |         | 21.6% (55/255)   | 26.6% (34/128)   |         |
| ≥35                                       | 32.4% (88/272)                                      | 18.9% (28/148)                            |         | 28.2% (72/255)   | 24.8% (32/128)   |         |
| <b>Race/Ethnicity</b>                     |   |   |         |  |  |         |
| American Indian or Alaska Native          | 0.4% (1/272)  | 0% (0/148)                                | <.0001  | 0.3% (1/255)   | 0% (0/128)   | .904    |
| Asian                                     | 1.1% (3/272)  | 0% (0/148)                                |         | 0.8% (2/255)   | 0% (0/128)   |         |
| Black or African American                 | 30.9% (84/272)                                      | 12.8% (19/148)                            |         | 24% (61/255)   | 28.1% (36/128)   |         |
| Hispanic                                  | 0.7% (2/272)  | 0.7% (1/148)                              |         | 0.5% (1/255)   | 0% (0/128)   |         |
| White                                     | 66.2% (180/272)                                     | 85.8% (127/148)                           |         | 73.7% (188/255)  | 71.2% (91/128)   |         |
| Other                                     | 0.7% (2/272)  | 0.7% (1/148)                              |         | 0.8% (2/255)   | 0.7% (1/128)   |         |
| <b>Current Smoker</b>                     | 16.5% (45/272)                                      | 14.9% (22/148)                            | .679    | 15.5% (40/255)   | 18.2% (23/128)   | .505    |
| <b>Neck circumference</b>                 | 47.6% (129/271)                                     | 41.5% (61/147)                            | .258    | 46.5% (119/255)  | 43.9% (56/128)   | .633    |
| <b>ASA Physical Status</b>                |   |   |         |  |  |         |
| ASA I                                     | 0.4% (1/262)  | 0.7% (1/145)                              | .390    | 0.7% (2/255)   | 0.7% (1/128)   | .750    |
| ASA II                                    | 42.4% (111/262)                                     | 35.9% (52/145)                            |         | 40.6% (103/255)  | 42.8% (55/128)   |         |
| ASA III                                   | 55% (144/262)                                       | 59.3% (86/145)                            |         | 56.4% (144/255)  | 54.1% (69/128)   |         |
| ASA IV                                    | 2.3% (6/262)  | 4.1% (6/145)                              |         | 2.3% (6/255)   | 2.3% (3/128)   |         |
| <b>Surgery Demographics</b>               |   |   |         |  |  |         |
| Surgical Patient                          | 94.1% (256/272)                                     | 95.9% (142/148)                           | .498    | 97.8% (249/255)  | 97% (124/128)  | .737    |
| High Risk Surgery                         | 4.8% (13/272)                                       | 7.4% (11/148)                             | .277    | 4.4% (11/255)  | 4.6% (6/128)   | .948    |
| Open Surgery                              | 7.7% (21/272)                                       | 12.8% (19/148)                            | .116    | 10.3% (26/255)   | 10% (13/128)   | .938    |
| <b>Length of Surgery (hr)</b>             |   |   |         |  |  |         |
| 0   | 5.9% (16/272)                                       | 4.1% (6/148)                              | .010    | 2.2% (6/255)   | 3% (4/128)   | .961    |
| <2  | 36.4% (99/272)                                      | 27% (40/148)                              |         | 34.9% (89/255)   | 33.4% (43/128)   |         |
| ≥2 - <4                                   | 44.1% (120/272)                                     | 48.6% (72/148)                            |         | 46.6% (119/255)  | 47.7% (61/128)   |         |

| Clinical Characteristic                                | Patient Characteristics before Propensity Weighting |   |         | Patient Characteristics after Propensity Weighting     |  |         |
|--|---|---|---------|--|--|---------|
|  | No Respiratory Depression Episode (n=272)           | ≥1 Respiratory Depression Episode (n=148) | p-value | No Respiratory Depression Episode (n=255) <sup>a</sup> | ≥1 Respiratory Depression Episode (n=128) <sup>a</sup> | p-value |
| ≥4   | 13.6% (37/272)                                      | 20.3% (30/148)                            |         | 16.3% (42/255)   | 16% (20/128)   |         |
| <b>Opioid Demographics</b>                             |   |   |         |  |  |         |
| Opioid Naive   | 68.8% (187/272)                                     | 79.1% (117/148)                           | .023    | 73% (186/255)  | 77.4% (99/128)   | .361    |
| Multiple Opioids or concurrent CNS/Sedating Medication | 98.9% (269/272)                                     | 98% (145/148)                             | .430    | 100% (255/255)   | 100% (128/128)   | N/A     |
| One opioid   | 2.6% (7/272)  | 2.7% (4/148)                              | .358    | 0.9% (2/255)   | 0.7% (1/128)   | .753    |
| Opioid number >1 - <4                                  | 49.6% (135/272)                                     | 56.8% (84/148)                            |         | 51.9% (132/255)  | 56.2% (72/128)   |         |
| Opioid number ≥4                                       | 47.8% (130/272)                                     | 40.5% (60/148)                            |         | 47.2% (120/255)  | 43.1% (55/128)   |         |
| <b>Cardiac Disorders</b>                               |   |   |         |  |  |         |
| Aortic Aneurysm  | 0.4% (1/272)  | 3.4% (5/148)                              | .022    | 0.3% (1/255)   | 1.4% (2/128)   | .260    |
| Aortic Valve Disease                                   | 0.4% (1/272)  | 0% (0/148)                                | 1       | 0.3% (1/255)   | 0% (0/128)   | 1       |
| Chronic Heart Failure                                  | 0.7% (2/272)  | 2% (3/147)                                | .349    | 0.9% (2/255)   | 1.2% (1/128)   | 1       |
| Coronary Artery Disease                                | 2.2% (6/272)  | 9.6% (14/146)                             | .001    | 6.1% (16/255)  | 5.4% (7/128)   | .781    |
| Hypertension   | 48.5% (132/272)                                     | 54.7% (81/148)                            | .261    | 51.1% (130/255)  | 51.7% (66/128)   | .909    |
| Mitral Valve Disease                                   | 1.8% (5/272)  | 0.7% (1/148)                              | .670    | 1.4% (4/255)   | 0.5% (1/128)   | .668    |
| Myocardial Infarction                                  | 0.7% (2/272)  | 4.1% (6/147)                              | .025    | 2.6% (7/255)   | 2.3% (3/128)   | 1       |
| Pulmonary Hypertension                                 | 0.7% (2/272)  | 0.7% (1/148)                              | 1       | 0% (0/255)   | 0% (0/128)   | ---     |
| <b>Sarcoidosis</b>                                     | 0.4% (1/272)  | 0% (0/148)                                | 1       | 0.4% (1/266)   | 0% (0/137)   | 1       |
| <b>Sepsis</b>  | 0.7% (2/272)  | 0.7% (1/148)                              | 1       | 0.3% (1/255)   | 0% (0/128)   | 1       |
| <b>Diabetes - Type I</b>                               | 1.5% (4/272)  | 3.4% (5/148)                              | .289    | 2.6% (7/255)   | 1.9% (2/128)   | .724    |
| <b>Diabetes - Type II</b>                              | 14% (38/272)  | 18.2% (27/148)                            | .261    | 15.8% (40/255)   | 18.3% (24/128)   | .534    |
| <b>Muscular Dystrophy</b>                              | 0.4% (1/272)  | 0.7% (1/148)                              | 1       | 0.4% (1/255)   | 0.5% (1/128)   | 1       |
| <b>Kidney Failure</b>                                  | 1.5% (4/272)  | 1.4% (2/148)                              | 1       | 1.2% (3/255)   | 0.8% (1/128)   | 1       |
| <b>Respiratory, Thoracic and Mediastinal Disorders</b> |   |   |         |  |  |         |
| Acute Bronchitis                                       | 2.6% (7/272)  | 1.4% (2/148)                              | .503    | 2.2% (6/255)   | 2.3% (3/128)   | 1       |
| Asthma   | 16.9% (46/272)                                      | 10.8% (16/148)                            | .113    | 13.7% (35/255)   | 16.1% (21/128)   | .996    |
| Chronic Bronchitis                                     | 0.7% (2/272)  | 0% (0/148)                                | .543    | 0.5% (1/255)   | 0% (0/128)   | 1       |
| Chronic Obstructive Pulmonary                          | 4.4% (12/272)                                       | 6.8% (10/148)                             | .360    | 5.8% (15/255)  | 4.4% (6/128)   | .556    |
| Chronic Restrictive Lung Disease                       | 0% (0/272)  | 0.7% (1/148)                              | .352    | 0% (0/255)   | 0% (0/128)   | ---     |
| Pneumonia  | 0.7% (2/272)  | 1.4% (2/148)                              | .616    | 0.8% (2/255)   | 0.9% (1/128)   | 1       |
| Pulmonary Fibrosis                                     | 0.4% (1/272)  | 0% (0/148)                                | 1       | 0.3% (1/255)   | 0% (0/128)   | 1       |
| <b>Sleep Disorders</b>                                 | 14.6% (39/268)                                      | 15.3% (22/144)                            | .885    | 14.3% (36/255)   | 12.9% (16/128)   | .708    |
| <b>Vascular Disorders</b>                              |   |   |         |  |  |         |
| Cerebral Aneurysm                                      | 0.7% (2/272)  | 2% (3/148)                                | .350    | 1.3% (3/255)   | 1.1% (1/128)   | .668    |
| Peripheral Vascular Disease                            | 1.8% (5/272)  | 2% (3/148)                                | 1       | 1.6% (4/255)   | 1.2% (2/128)   | 1       |
| Stroke   | 1.5% (4/272)  | 2.7% (4/147)                              | .459    | 1.7% (4/255)   | 1.6% (2/128)   | .265    |
| Transient Ischemic Attack                              | 0.7% (2/272)  | 2% (3/147)                                | .349    | 1% (3/255)   | 1.2% (2/128)   | 1       |
| <b>STOP BANG Score</b>                                 |   |   |         |  |  |         |

| Clinical Characteristic                    | Patient Characteristics before Propensity Weighting |   |         | Patient Characteristics after Propensity Weighting     |  |         |
|--|---|---|---------|--|--|---------|
|  | No Respiratory Depression Episode (n=272)           | ≥1 Respiratory Depression Episode (n=148) | p-value | No Respiratory Depression Episode (n=255) <sup>a</sup> | ≥1 Respiratory Depression Episode (n=128) <sup>a</sup> | p-value |
| Low Risk (0-2)                             | 48.9% (130/266)                                     | 37.1% (53/143)                            | .033    | 42.6% (109/255)  | 41.6% (53/128)   | .968    |
| Intermediate Risk (3-4)                    | 33.1% (88/266)                                      | 35.7% (51/143)                            |         | 37.1% (95/255)   | 37.2% (48/128)   |         |
| High Risk (5-8)                            | 18% (48/266)  | 27.3% (39/143)                            |         | 20.3% (52/255)   | 21.2% (27/128)   |         |
| <b>Procedure</b>                           |   |   |         |  |  |         |
| Bone and joint                             | 22.1% (60/272)                                      | 18.2% (27/148)                            | .158    | 20.4% (52/255)   | 18.8% (24/128)   | .978    |
| Gastrointestinal                           | 24.3% (66/272)                                      | 16.2% (24/148)                            |         | 21.8% (56/255)   | 18.3% (23/128)   |         |
| Hepatobiliary                              | 2.2% (6/272)  | 7.4% (11/148)                             |         | 2.8% (7/255)   | 4.1% (5/128)   |         |
| Medical                                    | 5.9% (16/272)                                       | 4.1% (6/148)                              |         | 2.2% (6/255)   | 3% (4/128)   |         |
| Nervous system, skull and spine            | 36% (98/272)  | 43.2% (64/148)                            |         | 42.3% (108/255)  | 44.1% (57/128)   |         |
| Obstetric and gynecological                | 5.5% (15/272)                                       | 6.8% (10/148)                             |         | 6.8% (17/255)  | 6.2% (8/128)   |         |
| Other                                      | 1.1% (3/272)  | 2.7% (4/148)                              |         | 1% (3/255)   | 1.4% (2/128)   |         |
| Renal and urinary tract                    | 0.4% (1/272)  | 0% (0/148)                                |         | 0.3% (1/255)   | 0 (0/128)  |         |
| Respiratory tract                          | 0.4% (1/272)  | 0% (0/148)                                |         | 0.3% (1/255)   | 0% (0/128)   |         |
| Therapeutic procedures and supportive care | 2.2% (6/272)  | 1.4% (2/148)                              |         | 2.1% (5/255)   | 4.1% (5/128)   |         |

<sup>a</sup>Patients missing any demographic or clinical data used excluded from propensity weighting

Abbreviations: ASA = American Society of Anesthesiologists; BMI = body mass index; CNS = central nervous system; SD= standard deviation; STOP BANG = Snoring, Tiredness, Observed apnea, blood Pressure, Body mass index, Age, Neck circumference and Gender