**Data Simulation Process**

The data will be simulated using R software based on summary statistics sourced from the clinical trial manuscript (Table 1:  **Patient characteristics by ethnicity or race,** and Figure 1: **Patient status by study day**).

The process is as follows :

1. ***Patient Characteristics by Ethnicity or Race*:** *Generate patient data variables for each ethnic or race group;*
2. ***Patient Characteristics by Day for each Ethnicity or Race Subsample****: For each ethnicity or race subsample, generate patient status by day.*
   1. *Required for each ethnic or race subsample data: Summary Statistics Day-level breakdown*

Then all ethnic or race group subsample data is stacked-up into one large dataset*.*

Below is an example of how each ethnic group’s data is generated in R.

**Other Patients:**

|  |  |  |
| --- | --- | --- |
|  | **Other** | **Simulation in R** |
| **Patients\*** | 51 (10.8%) | Ethnicity <- rep(“Other”, n) |
| **Age+** | 53.9 (15.6) | Age ~ Normal(n=51, mean = 53.9, sd = 15.6) |
| **Male** | 27 (52.9%) | Male ~ rbinom(n=51, 1, p = (0.52)); |
| **Tobacco use** |  |  |
| Former smoker | 17 (33.3%) | Former Smoker ~ rbinom(); |
| Current smoker | 11 (21.6%) | Current Smoker ~ rbinom(); |
| **Comorbidities** |  |  |
| Leukemia or lymphoma | 1 (2.0%) | Leukemia or lymphoma ~ rbinom(); |
| Metastatic cancer | 3 (5.9%) | Metastatic ~ rbinom(); |
| Immune suppression | 6 (11.8%) | Immune suppression ~ rbinom() |
| Cirrhosis | 3 (5.9%) | Cirrhosis ~ rbinom() |
| Diabetes | 16 (31.4%) | Diabetes ~rbinom() |
| Hypertension | 19 (37.3%) | Hypertension ~ rbinom() |
| Myocardial infarction | 6 (11.8%) | Myocardial infarction ~ rbinom() |
| Heart failure | 2 (3.9%) | Heart failure ~ rbinom() |
| Stroke | 2 (3.9%) | Stroke ~ rbinom() |
| Dementia | 1 (2.0%) | Dementia ~ rbinom() |
| Chronic lung disease | 11 (21.6%) | Chronic lung ~ rbinom() |
| Dialysis | 4 (7.8%) | Dialysis ~ rbinom() |
| **Body mass index+** | 28.3 (7.3) | BMI ~ rnorm(n, mean = 28.3, sd = 7.3) |
| **Baseline P/F ratio+** | 111.9 (39.9) | Baseline P/F ratio ~ rnorm(n, mean, sd) |
| **Neuromuscular Blockade** | 16 (31.4%) | Neuromuscular Blockade ~ rbinom(n) |

**Day-level Variables**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Deep Sedation (days 0 to 4)** | **All Days** | **Day 0** | **Day 1** | **Day 2** | **Day 3** | **Day 4** |
| Received deep sedation at any time | 48 (94.1%) |  |  |  |  |  |
| Proportion of days deeply sedated+ | 78.5 (29.9) |  |  |  |  |  |
| **Benzodiazepines (days 0 to 4)** |  |  |  |  |  |  |
| Received benzodiazepines  at any time | 21 (41.2%) |  |  |  |  |  |
| Proportion of days receiving benzodiazepines+ | 27.6 (37.8) |  |  |  |  |  |
| **SOFA score** *(Neuro excluded)*+ | 9.8 (3.8) |  |  |  |  |  |
| **APACHE score** *(All categories)*+ | 107.2 (30.0) |  |  |  |  |  |
| **APACHE score** *(GCS excluded)*+ | 78.9 (21.5) |  |  |  |  |  |
| **pH+** | 7.32 (0.11) |  |  |  |  |  |
| **Proportion of days 0 to 4 ventilated+** | 88.4 (19.9) |  |  |  |  |  |
| **Died within 90 Days** | 21 (41.2%) |  |  |  |  |  |
|  |  |  |  |  |  |  |

***Summary from Simulated Data***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Other** | **Black** | **Hispanic** | **White** |
| **Patients\*** | 51 (10.8%) | 70 (14.9%) | 48 (10.19%) |  |
| **Age+** | 53.9 (15.6) | 52.6 (14.9) | 57.0 (17.4) |  |
| **Male** | 27 (52.9%) | 30 (42.9%) | 22 (45.8%) |  |
| **Tobacco use** |  |  |  |  |
| Former smoker | 17 (33.3%) | 18 (25.8%) | 8 (16.7%) |  |
| Current smoker | 11 (21.6%) | 17 (24.3%) | 6 (12.5%) |  |
| **Comorbidities** |  |  |  |  |
| Leukemia or lymphoma | 1 (2.0%) | 3 (4.3%) | 1 (2.1%) |  |
| Metastatic cancer | 3 (5.9%) | 2 (4.3%) | 0 (0%) |  |
| Immune suppression | 6 (11.8%) | 6 (8.6%) | 5 (10.4%) |  |
| Cirrhosis | 3 (5.9%) | 7 (10%) | 9 (18.75%) |  |
| Diabetes | 16 (31.4%) | 23 (32.9%) | 15 (31.3%) |  |
| Hypertension | 19 (37.3%) | 39 (55.7%) | 24 (50%) |  |
| Myocardial infarction | 6 (11.8%) | 3 (4.3%) | 5 (10.4%) |  |
| Heart failure | 2 (3.9%) | 8 (11.4%) | 3 (6.3%) |  |
| Stroke | 2 (3.9%) | 4 (5.7%) | 5 (10.4%) |  |
| Dementia | 1 (2.0%) | 6 (8.6%) | 7 (14.6%) |  |
| Chronic lung disease | 11 (21.6%) | 11 (15.7%) | 5 (10.4%) |  |
| Dialysis | 4 (7.8%) | 8 (11.4%) | 1 (2.1%) |  |
| **Body mass index+** | 28.3 (7.3) | 30.0 (8.11) | 30 (8.11) |  |
| **Baseline P/F ratio+** | 111.9 (39.9) | 121.9 (36.9) | 106.9 (33.6) |  |
| **Neuromuscular Blockade** | 16 (31.4%) | 13 (18.6%) | 14 (29.2%) |  |

**Reference Summary Tables**

**Table 1: Patient characteristics by ethnicity or race**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Hispanic** | **White** | **Black** | **Other** | **All patients** |
| **Patients\*** | 48 (10.2%) | 302 (64.1%) | 70 (14.9%) | 51 (10.8%) | 471 (100%) |
| **Age+** | 54.4 (15.4) | 55.5 (16.4) | 53.2 (14.9) | 53.9 (15.6) | 54.8 (16.0) |
| **Male** | 25 (52.1%) | 158 (52.3%) | 39 (55.7%) | 27 (52.9%) | 249 (52.9%) |
| **Tobacco use** |  |  |  |  |  |
| Former smoker | 8 (16.7%) | 89 (29.5%) | 11 (15.7%) | 17 (33.3%) | 125 (26.5%) |
| Current smoker | 9 (18.8%) | 84 (27.8%) | 21 (30.0%) | 11 (21.6%) | 125 (26.5%) |
| **Comorbidities** |  |  |  |  |  |
| Leukemia or lymphoma | 3 (6.3%) | 13 (4.3%) | 3 (4.3%) | 1 (2.0%) | 20 (4.2%) |
| Metastatic cancer | 1 (2.1%) | 15 (5.0%) | 3 (4.3%) | 3 (5.9%) | 22 (4.7%) |
| Immune suppression | 10 (20.8%) | 53 (17.5%) | 10 (14.3%) | 6 (11.8%) | 79 (16.8%) |
| Cirrhosis | 8 (16.7%) | 24 (7.9%) | 5 (7.1%) | 3 (5.9%) | 40 (8.5%) |
| Diabetes | 17 (35.4%) | 81 (26.8%) | 23 (32.9%) | 16 (31.4%) | 137 (29.1%) |
| Hypertension | 22 (45.8%) | 142 (47.0%) | 37 (52.9%) | 19 (37.3%) | 220 (46.7%) |
| Myocardial infarction | 3 (6.3%) | 18 (6.0%) | 4 (5.7%) | 6 (11.8%) | 31 (6.6%) |
| Heart failure | 3 (6.3%) | 16 (5.3%) | 10 (14.3%) | 2 (3.9%) | 31 (6.6%) |
| Stroke | 4 (8.3%) | 9 (3.0%) | 4 (5.7%) | 2 (3.9%) | 19 (4.0%) |
| Dementia | 5 (10.4%) | 6 (2.0%) | 2 (2.9%) | 1 (2.0%) | 14 (3.0%) |
| Chronic lung disease | 5 (10.4%) | 61 (20.2%) | 9 (12.9%) | 11 (21.6%) | 86 (18.3%) |
| Dialysis | 2 (4.2%) | 6 (2.0%) | 6 (8.6%) | 4 (7.8%) | 18 (3.8%) |
| **Body mass index+** | 29.5 (8.2) | 32.7 (9.3) | 30.2 (9.2) | 28.3 (7.3) | 31.5 (9.1) |
| **Baseline P/F ratio+** | 114.4 (35.9) | 116.4 (39.2) | 105.2 (36.9) | 111.9 (39.9) | 114.0 (38.7) |
| **Neuromuscular Blockade** | 17 (35.4%) | 75 (24.8%) | 15 (21.4%) | 16 (31.4%) | 123 (26.1%) |
| **Deep Sedation (days 0 to 4)** |  |  |  |  |  |
| Received deep sedation at any time | 45 (93.8%) | 263 (87.1%) | 63 (90.0%) | 48 (94.1%) | 419 (89.0%) |
| Proportion of days deeply sedated+ | 85.8 (27.4) | 64.2 (35.9) | 61.4 (33.0) | 78.5 (29.9) | 67.5 (34.9) |
| **Benzodiazepines (days 0 to 4)** |  |  |  |  |  |
| Received benzodiazepines  at any time | 23 (47.9%) | 154 (51.0%) | 27 (38.6%) | 21 (41.2%) | 225 (47.8%) |
| Proportion of days receiving benzodiazepines+ | 33.4 (40.7) | 32.5 (38.9) | 21.0 (32.4) | 27.6 (37.8) | 30.3 (38.2) |
| **SOFA score** *(Neuro excluded)*+ | 10.3 (3.2) | 8.7 (3.3) | 9.3 (3.4) | 9.8 (3.8) | 9.0 (3.4) |
| **APACHE score** *(All categories)*+ | 115.5 (32.0) | 105.7 (29.8) | 106.0 (26.7) | 107.2 (30.0) | 106.8 (29.6) |
| **APACHE score** *(GCS excluded)*+ | 84.9 (24.6) | 77.1 (22.1) | 78.9 (21.0) | 78.9 (21.5) | 78.4 (22.2) |
| **pH+** | 7.30 (0.11) | 7.32 (0.10) | 7.33 (0.10) | 7.32 (0.11) | 7.32 (0.10) |
| **Proportion of days 0 to 4 ventilated+** | 93.9 (15.0) | 91.7 (17.0) | 92.4 (15.3) | 88.4 (19.9) | 91.6 (16.9) |
| **Died within 90 Days** | 25 (52.1%) | 125 (41.4%) | 25 (35.7%) | 21 (41.2%) | 196 (41.6%) |

*\* N (%) unless otherwise specified. Data are from 471 patients for whom complete sedation data were available.*

*+Mean (SD)*

**Figure 1: Patient status by study day**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Day 0** | **Day 1** | **Day 2** | **Day 3** | **Day 4** |  |
| **Deceased** | 7 | 39 | 56 | 69 | 80 |  |
| **Sedation Status Unknown** | 19 | 9 | 11 | 11 | 10 |  |
| **Deeply Sedated** | 345 | 314 | 258 | 229 | 203 |  |
| **Not Deeply Sedated** | 133 | 128 | 126 | 111 | 91 |  |
| **Extubated** | 1 | 15 | 54 | 85 | 121 |  |

***Legend:*** *Frequency and proportion of survival, sedation depth, and extubation during study days 0 through 4 for patients with ARDS in the control arm of the ROSE trial. The proportion of patients who died (black bars), remained mechanically ventilated with unknown sedation depth (gray bars), remained mechanically ventilated with deep sedation (dark blue bars), remained mechanically ventilated with light sedation (light blue bars) and were extubated (white bars) are displayed by study day. Deep sedation was defined as a day where the Richmond Agitation and Sedation Score was equal to or less than -2, the Riker Sedation Agitation Scale was equal to or greater than 1, or the Ramsay Sedation Scale was equal to or greater than 4.*