Supplementary

**Additional methods**

**Characteristics of the study dataset**

The data were prospectively collected and stored in two different databases. The Medical Information Mart for Intensive Care III database (MIMIC-III v1.4), is a freely accessible and conveniently-sized database that contains high resolution information from hospital monitoring systems (including laboratory data, medication, and hospital administrative data) and bedside monitoring systems (vital signs, caregivers notes, radiology reports). This database is hosted by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (MIT) and contains data for over 50,000 de-identified patient admissions to ICUs at the BIDMC from 2001 to 2012. We used the MIMIC Code Repository to define many concepts in MIMIC-III.

**Ethical approval**

The Institutional Review Board of the Beth Israel Deaconess Medical Center (2001-P-001699/14) and the Massachusetts Institute of Technology (No. 0403000206) approved use of the MIMIC database.

**Statistical analyses**

Relevant covariates known to predict outcome were entered into the multivariable model if a \( p \) value less than 0.1 was found in the univariable model and when the percentage of missing was less than 10%. In the adjusted models for the comparison of the groups (high vs. low spontaneous breathing and always vs. never spontaneous breathing), relevant covariates known to predict outcome were included, not considering variables with more than 10% of missing. In addition, ventilatory variables were not included in the model, since they are closely related to the types of ventilation studied and could mediate the relationship between them and outcomes. At the end, the following variables were considered: age, gender, weight, initial diagnosis, Elixhauser comorbidity score, use of vasopressor in the first day, limitation of support, SAPS II, OASIS, SOFA at day 1, heart rate at day 1 and 2, mean arterial pressure at day 1 and 2, and \( \text{SpO}_2/\text{FiO}_2 \) at day 1 and 2. All continuous variables were standardized before inclusion in the models to improve convergence. The use of neuromuscular blocking agents was not considered in the models due to its highly correlation with the variable of interest (spontaneous breathing).
Table S1 Classification of ventilation modes in the MIMIC-III dataset

| Original Classification | Re–classification | Mode Mandating Spontaneous Breathing |
|-------------------------|-------------------|-------------------------------------|
| APRV                    | Airway Pressure Release Ventilation (APRV) | No |
| APRV/Biphasic+ApnVol    | Airway Pressure Release Ventilation (APRV) | No |
| Assist Control          | Assist Control    | No |
| CMV                     | Continuous Mandatory Ventilation | No |
| CMV/ASSIST              | Continuous Mandatory Ventilation | No |
| CMV/ASSIST/AutoFlow     | Pressure Regulated Volume Control (PRVC) | No |
| CMV/AutoFlow            | Pressure Regulated Volume Control (PRVC) | No |
| CPAP                    | Continuous Positive Airway Pressure (CPAP) | Yes |
| CPAP/PSV                | Proportional Assist Ventilation (PAV) | Yes |
| CPAP/PSV+Apn TCPL       | Pressure Support Ventilation (PSV) | Yes |
| CPAP/PSV+ApnPres        | Pressure Support Ventilation (PSV) | Yes |
| CPAP/PSV+ApnVol         | Pressure Support Ventilation (PSV) | Yes |
| CPAP+PS                 | Pressure Support Ventilation (PSV) | Yes |
| MMV                     | Mandatory Minute Ventilation (MMV) | No |
| MMV/AutoFlow            | Mandatory Minute Ventilation (MMV) | No |
| MMV/PSV                 | Mandatory Minute Ventilation–PSV (MMV–PSV) | No |
| MMV/PSV/AutoFlow        | Mandatory Minute Ventilation–PSV (MMV–PSV) | No |
| Other/Remarks            | Other | No |
| PCV+                    | Pressure Control | No |
| PCV+/PSV                | Pressure Control | No |
| PCV+Assist              | Pressure Control | No |
| PRES/AC                 | Pressure Control | No |
| Pressure Control         | Pressure Control | No |
| Pressure Support         | Pressure Support Ventilation (PSV) | Yes |
| PRVC/AC                 | Pressure Regulated Volume Control (PRVC) | No |
| PSV/SBT                 | Pressure Support Ventilation (PSV) | Yes |
| SIMV                    | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| SIMV/AutoFlow           | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| SIMV/PSV                | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| SIMV/PSV/AutoFlow       | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| SIMV+PS                 | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| Standby                 | Other | No |
| SYNCHRON MASTER         | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| SYNCHRON SLAVE          | Synchronized Intermittent Mandatory Ventilation (SIMV) | No |
| TCPCV                   | Pressure Control | No |
| VOL/AC                  | Volume Control | No |
| ID | Moment | Set Lowest RR | Total Lowest RR | Set Highest RR | Total Highest RR | SA | Percentage of SB |
|----|--------|---------------|-----------------|---------------|-----------------|----|-----------------|
| 01 | 1      | 10            | 10              | 23            | 23              | No |                 |
| 01 | 2      | 9             | 9               | 25            | 25              | No |                 |
| 01 | 3      | 10            | 12              | 29            | 31              | Yes|                 |
| 01 | 4      | 13            | 13              | 25            | 28              | Excluded | $\frac{N_M \cdot SB}{N_O} \times \left( \frac{3}{6} \right) \times 100 = 50\%$ |
| 01 | 5      | 12            | 14              | 22            | 25              | Yes|                 |
| 01 | 6      | 12            | 14              | 24            | 24              | Excluded |                     |
| 01 | 7      | 12            | 15              | 23            | 24              | Yes|                 |
| 01 | 8      | 10            | 10              | 21            | 21              | No |                 |
| 02 | 1      | 10            | 10              | 22            | 23              | Excluded |                     |
| 02 | 2      | 14            | 14              | 25            | 25              | No |                 |
| 02 | 3      | 17            | 17              | 28            | 28              | No |                 |
| 02 | 4      | 9             | 9               | 25            | 25              | No | $\frac{N_M \cdot SB}{N_O} \times \left( \frac{0}{7} \right) \times 100 = 0\%$ |
| 02 | 5      | 11            | 11              | 24            | 24              | No |                 |
| 02 | 6      | 10            | 10              | 26            | 26              | No |                 |
| 02 | 7      | 11            | 11              | 29            | 29              | No |                 |
| 02 | 8      | 12            | 12              | 30            | 30              | No |                 |

ID: unique identifier; RR: respiratory rate; SB: spontaneous breathing; $N_M \cdot SB$: number of moments with spontaneous breathing; $N_O$: number of observations available.
Figure S1 Flowchart of the study in the MIMIC-III dataset.
**Table S3 Vital signs and laboratory tests**

|                                | High Spontaneous Breathing (n=2374) | Low Spontaneous Breathing (n=1006) | Absolute Difference* (95% Confidence Interval) | P value |
|--------------------------------|-------------------------------------|------------------------------------|-----------------------------------------------|---------|
| **First day of ventilation**   |                                     |                                    |                                               |         |
| SAS                            | 3.0 (2.8–3.4)                       | 3.0 (2.3–3.3)                      | 0.26 (0.19 to 0.33)                           | < 0.001 |
| Heart rate, bpm                | 92 (80–104)                         | 92 (80–103)                        | 0.18 (-0.96 to 1.33)                          | 0.753   |
| Mean arterial pressure, mmHg   | 80 (73–89)                          | 81 (73–90)                         | -0.55 (-1.49 to 0.40)                         | 0.257   |
| SpO₂, %                        | 96 (94–98)                          | 96 (94–98)                         | 0.31 (0.05 to 0.57)                           | 0.021   |
| Temperature, °C                | 37.1 (36.6–37.7)                    | 37.0 (36.4–37.4)                   | 0.19 (0.14 to 0.25)                           | < 0.001 |
| pH                             | 7.38 (7.33–7.42)                    | 7.36 (7.31–7.40)                   | 0.02 (0.01 to 0.03)                           | < 0.001 |
| PaO₂/FiO₂                      | 258 (185–361)                       | 264 (186–367)                      | -2.94 (-11.84 to 5.98)                        | 0.517   |
| SpO₂/FiO₂                      | 176 (140–209)                       | 163 (137–197)                      | 6.81 (3.97 to 9.65)                           | < 0.001 |
| PaCO₂, mmHg                    | 39 (35–44)                          | 40 (36–45)                         | -1.01 (-1.67 to -0.35)                        | 0.003   |
| **Second day of ventilation**  |                                     |                                    |                                               |         |
| SAS                            | 3.1 (3.0–3.7)                       | 3.0 (2.5–3.3)                      | 0.31 (0.24 to 0.38)                           | < 0.001 |
| Heart rate, bpm                | 90 (79–102)                         | 89 (78–100)                        | 1.45 (0.35 to 2.56)                           | 0.010   |
| Mean arterial pressure, mmHg   | 81 (73–90)                          | 80 (73–90)                         | 0.08 (-0.75 to 0.90)                          | 0.856   |
| SpO₂, %                        | 97 (95–98)                          | 97 (95–98)                         | -0.05 (-0.27 to 0.17)                         | 0.648   |
| Temperature, °C                | 37.3 (36.8–37.8)                    | 37.2 (36.7–37.7)                   | 0.10 (0.06 to 0.15)                           | < 0.001 |
| pH                             | 7.40 (7.36–7.43)                    | 7.41 (7.36–7.44)                   | -0.01 (-0.01 to 0.00)                         | 0.019   |
| PaO₂/FiO₂                      | 247 (187–324)                       | 243 (186–321)                      | 1.62 (-5.19 to 8.46)                          | 0.643   |
| SpO₂/FiO₂                      | 213 (184–244)                       | 207 (176–244)                      | 3.30 (0.17 to 6.44)                           | 0.039   |
| PaCO₂, mmHg                    | 39 (34–44)                          | 38 (34–42)                         | 0.81 (0.19 to 1.42)                           | 0.010   |

Data are median (quartile 25% - quartile 75%). SpO₂: pulse oximetry; SAS: sedation agitation scale. *mean difference from a univariable mixed-effect linear model with year as random effect.
Figure S2 Comparison of set and total respiratory rate among groups. Symbols and bars are mean and 95% confidence interval. Mixed-effect longitudinal models with random intercept for patients and year of admission, and with group, time and the interaction of group x time as fixed effects. P values reported are for the group and reflect the overall test for difference between groups across the 48 hours.

Table S4 Unadjusted analyses for the primary and secondary outcomes

|                                | High Spontaneous Breathing (n=2374) | Low Spontaneous Breathing (n=1006) | Absolute Difference* (95% Confidence Interval) | P value |
|--------------------------------|-------------------------------------|------------------------------------|-------------------------------------------------|---------|
| Ventilator–free days at day 28 | 20.0 (0.0–24.2)                     | 19.0 (0.00–23.7)                   | 0.19 (-0.59 to 0.97)*                             | 0.635   |
| Duration of ventilation in survivors, days | 6.5 (3.6–12.2)                     | 7.6 (4.1–13.9)                     | -1.03 (-1.90 to -0.15)*                           | 0.021   |
| ICU length of stay, days      | 9.5 (5.8–15.7)                      | 10.0 (6.0–17.1)                    | -0.80 (-1.57 to -0.02)*                           | 0.043   |
| Hospital length of stay, days | 15.4 (9.6–24.2)                     | 15.8 (9.3–25.3)                    | -0.81 (-1.97 to 0.35)*                            | 0.170   |
| ICU mortality                 | 598 (25.2)                          | 246 (24.5)                         | 0.74 (-2.46 to 3.93)*                             | 0.651   |
| Hospital mortality            | 712 (30.0)                          | 281 (27.9)                         | 2.06 (-1.30 to 5.42)*                             | 0.230   |
| 30-day mortality              | 696 (29.3)                          | 280 (27.8)                         | 1.48 (-1.86 to 4.83)*                             | 0.384   |

Data are median (quartile 25% - quartile 75%) or N (percentage). ICU: intensive care unit; *absolute difference from a univariable mixed-effect linear model with year as random effect; †effect estimate is mean difference; ‡effect estimate is risk ratio.

Figure S3 Subgroup analyses.
|                                | Always Spontaneous Breathing (n=1809) | Never Spontaneous Breathing (n=755) | P value |
|--------------------------------|---------------------------------------|-------------------------------------|---------|
| Age, years                     | 67.5 (54.0–78.3)                      | 61.8 (47.3–74.9)                    | < 0.001 |
| Male gender                    | 977 (54.0)                            | 454 (60.1)                          | 0.005   |
| Weight, kg                     | 77.0 (65.5–92.8)                      | 81.1 (68.3–98.6)                    | < 0.001 |
| Height, cm                     | 170 (164–177)                         | 173 (163–178)                       | 0.001   |
| Body mass index, kg/m²         | 27.3 (23.8–32.2)                      | 28.3 (24.2–33.2)                    | 0.011   |
| Predicted body weight, kg      | 63.9 (54.7–73.1)                      | 66.2 (56.9–73.1)                    | 0.001   |
| Admission type                 |                                       |                                     | 0.032   |
| Surgical elective              | 136 (7.5)                             | 61 (8.1)                            |         |
| Surgical urgency               | 89 (4.9)                              | 20 (2.6)                            |         |
| Clinical                       | 1584 (87.6)                           | 674 (89.3)                          |         |
| Source of admission            |                                       |                                     | 0.024   |
| Emergency room                 | 881 (48.7)                            | 383 (50.7)                          |         |
| Office or operating room       | 195 (10.8)                            | 81 (10.7)                           |         |
| Ward or step-down unit         | 235 (13.0)                            | 125 (16.6)                          |         |
| Transferred from other hospital| 482 (26.6)                            | 163 (21.6)                          |         |
| Other                          | 16 (0.9)                              | 3 (0.1)                             |         |
| Initial diagnosis              |                                       |                                     | < 0.001 |
| Sepsis (including pneumonia)   | 404 (22.3)                            | 132 (17.5)                          |         |
| Cardiovascular disease         | 377 (20.8)                            | 221 (29.3)                          |         |
| Other respiratory condition    | 279 (15.4)                            | 95 (12.6)                           |         |
| Neurological condition         | 332 (18.4)                            | 152 (20.1)                          |         |
| Renal condition                | 27 (1.5)                              | 1 (0.1)                             |         |
| Other                          | 390 (21.6)                            | 154 (20.4)                          |         |
| COPD                           | 102 (5.6)                             | 35 (4.6)                            | 0.351   |
| Smoking                        | 857 (48.0)                            | 344 (46.9)                          | 0.018   |
| Elixhauser comorbidity score   | 6 (2–12)                              | 6 (0–11)                            | 0.026   |
| Support in the first 24 hours  |                                       |                                     |         |
| Vasopressor                    | 818 (45.2)                            | 444 (58.8)                          | < 0.001 |
| Renal replacement therapy      | 99 (5.5)                              | 35 (4.6)                            | 0.441   |
| Limitation of support          | 461 (27.2)                            | 155 (22.0)                          | 0.009   |
| Severity of illness            |                                       |                                     |         |
| SAPS II                        | 43 (34–53)                            | 43 (33–55)                          | 0.858   |
| OASIS                          | 38 (33–44)                            | 37 (32–43)                          | 0.001   |
| SOFA                           | 6 (4–8)                               | 7 (4–9)                             | < 0.001 |

Data are median (quartile 25% - quartile 75%) or No (%). BMI: body mass index; PBW: predicted body weight; COPD: chronic obstructive pulmonary disease; ARDS: acute respiratory distress syndrome; SAPS: Simplified Acute Physiology Score; OASIS: Oxford Acute Severity of Illness Score; SOFA: Sequential Organ Failure Assessment; bpm: beats per minute.
Table S6  Vital signs and laboratory tests according to more strict groups

|                                      | Always Spontaneous Breathing (n=1809) | Never Spontaneous Breathing (n=755) | Absolute Difference* (95% Confidence Interval) | P value |
|--------------------------------------|---------------------------------------|-------------------------------------|-------------------------------------------------|---------|
| First day of ventilation             |                                       |                                     |                                                 |         |
| SAS                                  | 3.0 (2.9–3.4)                         | 3.0 (2.2–3.2)                       | 0.34 (0.26 to 0.42)                             | < 0.001 |
| Heart rate, bpm                      | 92 (81–104)                           | 92 (79–104)                         | 0.38 (-0.94 to 1.71)                            | 0.573   |
| Mean arterial pressure, mmHg         | 80 (73–89)                            | 81 (73–90)                          | -0.81 (-1.91 to 0.29)                           | 0.149   |
| SpO\textsubscript{2}, %              | 96 (94–98)                            | 96 (94–98)                          | 0.42 (0.11 to 0.73)                             | 0.007   |
| Temperature, °C                      | 37.2 (36.6–37.7)                      | 36.9 (36.4–37.4)                    | 0.24 (0.18 to 0.30)                             | < 0.001 |
| pH                                   | 7.38 (7.33–7.42)                      | 7.36 (7.31–7.40)                    | 0.02 (0.02 to 0.03)                             | < 0.001 |
| PaO\textsubscript{2}/FiO\textsubscript{2} | 261 (186–366)                        | 260 (184–366)                       | 2.46 (-7.82 to 12.78)                           | 0.640   |
| SpO\textsubscript{2}/FiO\textsubscript{2} | 178 (141–210)                        | 161 (136–196)                       | 9.66 (6.38 to 12.96)                            | < 0.001 |
| PaCO\textsubscript{2}, mmHg          | 39 (34–44)                            | 40 (36–44)                          | -1.20 (-1.93 to -0.46)                          | 0.001   |
| Second day of ventilation            |                                       |                                     |                                                 |         |
| SAS                                  | 3.1 (3.0–3.7)                         | 3.0 (2.2–3.3)                       | 0.39 (0.30 to 0.47)                             | < 0.001 |
| Heart rate, bpm                      | 90 (79–102)                           | 89 (78–101)                         | 1.28 (0.01 to 2.55)                             | 0.048   |
| Mean arterial pressure, mmHg         | 80 (73–90)                            | 80 (73–89)                          | 0.13 (-0.82 to 1.08)                            | 0.786   |
| SpO\textsubscript{2}, %              | 97 (95–98)                            | 97 (95–98)                          | -0.02 (-0.28 to 0.24)                           | 0.888   |
| Temperature, °C                      | 37.3 (36.9–37.8)                      | 37.2 (36.7–37.7)                    | 0.11 (0.06 to 0.17)                             | < 0.001 |
| pH                                   | 7.40 (7.36–7.43)                      | 7.41 (7.36–7.44)                    | -0.01 (-0.01 to 0.00)                           | 0.057   |
| PaO\textsubscript{2}/FiO\textsubscript{2} | 247 (187–325)                        | 238 (182–319)                       | 4.12 (-3.76 to 12.04)                           | 0.307   |
| SpO\textsubscript{2}/FiO\textsubscript{2} | 213 (184–244)                        | 199 (175–242)                       | 5.75 (2.12 to 9.40)                             | 0.002   |
| PaCO\textsubscript{2}, mmHg          | 38 (34–44)                            | 38 (34–42)                          | 0.67 (-0.03 to 1.36)                            | 0.060   |

Data are median (quartile 25% - quartile 75%). SpO\textsubscript{2}: pulse oximetry; SAS: sedation agitation scale; * mean difference from a univariable mixed-effect linear model with year as random effect.
Table S7 Ventilatory characteristics of the patients included according to more strict groups

|                           | Always Spontaneous Breathing (n=1809) | Never Spontaneous Breathing (n=755) | Absolute Difference*** (95% Confidence Interval) | P value |
|---------------------------|--------------------------------------|-------------------------------------|--------------------------------------------------|---------|
| Percentage of spontaneous breathing | 100 (100–100)                        | 0 (0–0)                             | –                                                | –       |
| First day of ventilation  |                                      |                                     |                                                  |         |
| Tidal volume, ml/kg PBW   | 8.9 (7.9–10.1)                       | 8.8 (7.9–10.0)                     | 0.09 (-0.07 to 0.25)                              | 0.249   |
| PEEP, cmH\textsubscript{2}O | 5 (5–7)                              | 6 (5–10)                           | -0.87 (-1.07 to -0.68)                            | <0.001  |
| Peak pressure, cmH\textsubscript{2}O | 24 (20–29)                          | 28 (24–33)                         | -3.59 (-4.06 to -3.13)                            | <0.001  |
| Driving pressure, cmH\textsubscript{2}O | 14 (11–17)                         | 15 (12–17)                         | -0.89 (-1.22 to -0.56)                            | <0.001  |
| Respiratory rate, mpm     | 20 (18–24)                           | 19 (17–21)                         | 1.76 (1.35 to 2.17)                               | <0.001  |
| Mechanical power, J/min\textsuperscript{*} | 23.3 (17.6–30.6)                   | 24.1 (18.5–31.5)                   | -0.85 (-1.78 to 0.09)                             | 0.076   |
| Minute ventilation, L/min | 12.1 (10.2–14.3)                     | 11.1 (9.6–12.8)                    | 1.00 (0.70 to 1.31)                              | <0.001  |
| FiO\textsubscript{2}, %     | 55 (45–70)                           | 60 (50–70)                         | -2.69 (-3.68 to -1.70)                            | <0.001  |
| Second day of ventilation |                                      |                                     |                                                  |         |
| Tidal volume, ml/kg PBW   | 8.7 (7.6–9.8)                        | 8.6 (7.6–9.6)                      | 0.03 (-0.12 to 0.19)                              | 0.651   |
| PEEP, cmH\textsubscript{2}O | 5 (5–8)                              | 7 (5–10)                           | -1.07 (-1.33 to -0.81)                            | <0.001  |
| Peak pressure, cmH\textsubscript{2}O | 24 (20–29)                          | 28 (24–32)                         | -3.48 (-3.96 to -3.00)                            | <0.001  |
| Driving pressure, cmH\textsubscript{2}O | 13 (11–16)                         | 14 (12–16)                         | -0.63 (-0.95 to -0.32)                            | <0.001  |
| Respiratory rate, mpm     | 20 (17–23)                           | 18 (15–21)                         | 1.71 (1.32 to 2.10)                               | <0.001  |
| Mechanical power, J/min\textsuperscript{*} | 21.0 (15.7–27.8)                    | 21.6 (16.5–27.9)                   | -0.38 (-1.14 to 0.38)                             | 0.325   |
| Minute ventilation, L/min | 11.3 (9.4–13.4)                      | 10.3 (8.6–12.3)                    | 1.04 (0.78 to 1.29)                               | <0.001  |
| FiO\textsubscript{2}, %     | 45 (40–50)                           | 50 (40–55)                         | -1.46 (-2.37 to -0.56)                            | 0.002   |

Data are median (quartile 25% - quartile 75%). PEEP: positive end-expiratory pressure; FiO\textsubscript{2}: inspired fraction of oxygen; \* calculated when plateau pressure is available and as: plateau pressure – PEEP; ** calculated when plateau pressure is available and as: 0.098× tidal volume × respiratory rate ×(peak pressure – driving pressure/2); *** mean difference from a univariable mixed–effect linear model with year as random effect.
Figure S4 Comparison of set and total respiratory rate among more strict groups. Symbols and bars are mean and 95% confidence interval. Mixed-effect longitudinal models with random intercept for patients and year of admission, and with group, time and the interaction of group x time as fixed effects. P values reported are for the group and reflect the overall test for difference between groups across the 48 hours.
Figure S5 Measurements of ventilatory parameters every 6 hours for the first 48 hours of ventilation according to more strict groups. Circles and bars are mean and 95% confidence interval. Mixed-effect longitudinal models with random intercept for patients and with group, time and the interaction of group x time as fixed effects. P values for the group reflect the overall test for difference between groups across the 48 hours while P values for the group x time interaction evaluate if change over time differed by group.
### Table S8 Unadjusted analyses for the primary and secondary outcomes according to more strict groups

|                               | Always Spontaneous Breathing (n=1809) | Never Spontaneous Breathing (n=755) | Absolute Difference* (95% Confidence Interval) | P value |
|-------------------------------|---------------------------------------|-------------------------------------|-----------------------------------------------|---------|
| Ventilator–free days at day 28| 20 (0–24)                             | 18 (0–23)                           | 0.72 (-0.19 to 1.63)                          | 0.119   |
| Duration of ventilation in    | 5.9 (3.6–10.4)                        | 5.0 (2.9–9.8)                       | 0.80 (-0.03 to 1.63)                          | 0.058   |
| survivors, days               |                                       |                                     |                                               |         |
| ICU length of stay, days      | 9.5 (5.9–15.6)                        | 10.1 (6.0–17.4)                     | -1.04 (-1.92 to -0.14)                        | 0.022   |
| Hospital length of stay, days | 15.5 (9.7–24.4)                       | 15.4 (9.2–25.8)                     | -0.83 (-2.20 to 0.55)                         | 0.235   |
| ICU mortality                 | 470 (26.0)                            | 203 (26.9)                          | -0.91 (-4.64 to 2.83)                         | 0.635   |
| Hospital mortality            | 561 (31.0)                            | 229 (30.3)                          | 0.68 (-3.24 to 4.60)                          | 0.734   |
| 30–day mortality              | 546 (30.2)                            | 230 (30.5)                          | -0.28 (-4.18 to 3.62)                         | 0.888   |

Data are median (quartile 25% - quartile 75%) or N (percentage). ICU: intensive care unit. * absolute difference from a univariable mixed-effect linear model with year as random effect; effect estimate is mean difference; effect estimate is risk ratio.

### Table S9 Adjusted analyses for the primary and secondary outcomes according to more strict groups

|                               | Always Spontaneous Breathing (n=1809) | Never Spontaneous Breathing (n=755) | Absolute Difference*;** (95% Confidence Interval) | P value |
|-------------------------------|---------------------------------------|-------------------------------------|-----------------------------------------------|---------|
| Ventilator–free days at day 28| 20 (0–24)                             | 18 (0–23)                           | 0.96 (0.20 to 1.72)                           | 0.014   |
| Duration of ventilation in    | 5.9 (3.6–10.4)                        | 5.0 (2.9–9.8)                       | 0.77 (-0.16 to 1.70)                          | 0.109   |
| survivors, days               |                                       |                                     |                                               |         |
| ICU length of stay, days      | 9.5 (5.9–15.6)                        | 10.1 (6.0–17.4)                     | -0.86 (-1.83 to 0.10)                         | 0.080   |
| Hospital length of stay, days | 15.5 (9.7–24.4)                       | 15.4 (9.2–25.8)                     | -0.29 (-1.74 to 1.17)                         | 0.700   |
| ICU mortality                 | 470 (26.0)                            | 203 (26.9)                          | -1.27 (-4.40 to 1.86)                         | 0.428   |
| Hospital mortality            | 561 (31.0)                            | 229 (30.3)                          | -1.02 (-4.19 to 2.13)                         | 0.530   |
| 30–day mortality              | 546 (30.2)                            | 230 (30.5)                          | -1.66 (-4.86 to 1.54)                         | 0.313   |

Data are median (quartile 25% - quartile 75%) or N (percentage). ICU: intensive care unit. * absolute difference from a multivariable mixed-effect linear model with year as random effect and adjusted for: age, gender, weight, initial diagnosis, Elixhauser comorbidity score, use of vasopressor in the first day, limitation of support, SAPS II, OASIS, SOFA at day 1, heart rate at day 1 and 2, mean arterial pressure at day 1 and 2, and SpO2 / FiO2 at day 1 and 2; ** continuous variables were standardized before inclusion to improve convergence; effect estimate is mean difference; effect estimate is risk ratio.