

## Supplementary Material

**Table S1.** List of ICD-10 codes used to identify comorbidities

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|                                                                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------|
| Bronchial asthma: J45, J46                                                                                                                         |
| COPD: J44                                                                                                                                          |
| Pneumonia: A481, J100, J110, J12, J13, J14, J15, J16, J170, J178, J18, J85, J86                                                                    |
| Mycotic infection: A420, A43, B37, B380, B381, B382, B390, B391, B392, B400, B401, B402, B410, B420, B440, B441, B449, B460, J172                  |
| Pulmonary embolism: I26                                                                                                                            |
| Bronchiectasis: J40, J41, J42, J47                                                                                                                 |
| Pneumothorax: J93, J94                                                                                                                             |
| Cor pulmonale: I27                                                                                                                                 |
| Lung cancer: C34                                                                                                                                   |
| Other types of cancer: C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24 |
| Disseminated intravascular coagulation: D65                                                                                                        |
| Chronic heart failure: I50                                                                                                                         |
| Tachycardia: I47, I48, I49, R000, T818                                                                                                             |
| Acute coronary syndrome: I20, I21, I22, I23, I24, I25                                                                                              |
| Diabetes mellitus: E11                                                                                                                             |
| Stroke: I60, I61, I62, I63, I64, I65, I66, I67, I68, I69                                                                                           |
| Dementia: G30, F01, F03, F107                                                                                                                      |
| Renal failure: E102, E112, E142, I120, N17, N18, N19                                                                                               |
| Liver dysfunction: B89, B181, B182, B659, B661, K70, K71, K72, K73, K74, K76                                                                       |
| Gastroesophageal reflux disease: K21                                                                                                               |

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ICD, the International Classification of Diseases, 10th revision; COPD, chronic obstructive pulmonary disease

**Table S2.** Baseline characteristics of patients before and after stabilized IPTW using propensity scores in the sensitivity analyses 1

| Characteristics                       | All patients                               |      |                                         |      |      | Patients after IPTW estimation             |      |                                         |      |       |
|---------------------------------------|--------------------------------------------|------|-----------------------------------------|------|------|--------------------------------------------|------|-----------------------------------------|------|-------|
|                                       | High-dose corticosteroid group (n = 15240) | %    | Low-dose corticosteroid group (n = 221) | %    | SMD  | High-dose corticosteroid group (n = 15241) | %    | Low-dose corticosteroid group (n = 220) | %    | SMD   |
| Male sex                              | 10584                                      | 69.4 | 153                                     | 69.2 | −0.5 | 10584                                      | 69.4 | 152                                     | 69.1 | −0.9  |
| Age, years                            |                                            |      |                                         |      |      |                                            |      |                                         |      |       |
| 15–70                                 | 4249                                       | 27.9 | 57                                      | 25.8 | −4.7 | 4245                                       | 27.9 | 56                                      | 25.5 | −5.0  |
| 71–80                                 | 6161                                       | 40.4 | 80                                      | 36.2 | −8.7 | 6152                                       | 40.4 | 102                                     | 46.4 | 11.7  |
| ≥80                                   | 4719                                       | 31.0 | 82                                      | 37.1 | 13.0 | 4732                                       | 31.0 | 61                                      | 27.7 | −7.5  |
| Missing                               | 111                                        | 0.7  | 2                                       | 0.9  | 2.0  | 111                                        | 0.7  | 1                                       | 0.5  | −2.0  |
| Treatment year                        |                                            |      |                                         |      |      |                                            |      |                                         |      |       |
| 2010–2011                             | 2484                                       | 16.3 | 30                                      | 13.6 | −7.6 | 2478                                       | 16.3 | 37                                      | 16.8 | 2.0   |
| 2012–2013                             | 3373                                       | 22.1 | 48                                      | 21.7 | −1.0 | 3372                                       | 22.1 | 44                                      | 20.0 | −5.4  |
| 2014–2015                             | 4284                                       | 28.1 | 65                                      | 29.4 | 2.9  | 4287                                       | 28.1 | 60                                      | 27.3 | −2.2  |
| 2016–2017                             | 5099                                       | 33.5 | 78                                      | 35.3 | 3.9  | 5103                                       | 33.5 | 79                                      | 35.9 | 5.2   |
| BMI (kg/m <sup>2</sup> )              |                                            |      |                                         |      |      |                                            |      |                                         |      |       |
| <23                                   | 7975                                       | 52.3 | 127                                     | 57.5 | 10.3 | 7986                                       | 52.4 | 112                                     | 50.9 | −3.0  |
| 23–25                                 | 2750                                       | 18.0 | 37                                      | 16.7 | −3.4 | 2747                                       | 18.0 | 48                                      | 21.8 | 9.6   |
| ≥25                                   | 2820                                       | 18.5 | 38                                      | 17.2 | −3.4 | 2817                                       | 18.5 | 39                                      | 17.7 | −1.5  |
| Missing                               | 1695                                       | 11.1 | 19                                      | 8.6  | −8.5 | 1690                                       | 11.1 | 21                                      | 9.5  | −5.9  |
| Hugh–Jones dyspnea score on admission |                                            |      |                                         |      |      |                                            |      |                                         |      |       |
| 1–2                                   | 1940                                       | 12.7 | 26                                      | 11.8 | −2.9 | 1938                                       | 12.7 | 26                                      | 11.8 | −3.4  |
| 3                                     | 1232                                       | 8.1  | 19                                      | 8.6  | 1.9  | 1233                                       | 8.1  | 18                                      | 8.2  | 1.0   |
| 4                                     | 2775                                       | 18.2 | 38                                      | 17.2 | −2.7 | 2773                                       | 18.2 | 48                                      | 21.8 | 9.1   |
| 5                                     | 6008                                       | 39.4 | 82                                      | 37.1 | −4.8 | 6003                                       | 39.4 | 71                                      | 32.3 | −14.6 |
| Missing                               | 3285                                       | 21.6 | 56                                      | 25.3 | 8.9  | 3294                                       | 21.6 | 57                                      | 25.9 | 9.9   |

|                                               |       |      |     |      |       |       |      |     |      |      |
|-----------------------------------------------|-------|------|-----|------|-------|-------|------|-----|------|------|
| Japan Coma Scale score on admission           |       |      |     |      |       |       |      |     |      |      |
| 0- or 1-digit (alert or dull)                 | 14830 | 97.3 | 211 | 95.5 | −9.9  | 14827 | 97.3 | 214 | 97.3 | 0.8  |
| 2-digit (somnolence)                          | 232   | 1.5  | 2   | 0.9  | −5.6  | 231   | 1.5  | 3   | 1.4  | −1.1 |
| 3-digit (coma)                                | 178   | 1.2  | 8   | 3.6  | 16.1  | 183   | 1.2  | 3   | 1.4  | 0    |
| Charlson comorbidity index                    |       |      |     |      |       |       |      |     |      |      |
| 0                                             | 8749  | 57.4 | 112 | 50.7 | −13.5 | 8735  | 57.3 | 127 | 57.7 | 0.3  |
| 1                                             | 1159  | 7.6  | 29  | 13.1 | 18.2  | 1171  | 7.7  | 14  | 6.4  | −4.4 |
| 2                                             | 3548  | 23.3 | 53  | 24.0 | 1.7   | 3550  | 23.3 | 48  | 21.8 | −3.5 |
| ≥3                                            | 1784  | 11.7 | 27  | 12.2 | 1.6   | 1785  | 11.7 | 31  | 14.1 | 7.3  |
| Smoking index, pack-years                     |       |      |     |      |       |       |      |     |      |      |
| 0                                             | 6966  | 45.7 | 106 | 48.0 | 4.5   | 6971  | 45.7 | 98  | 44.5 | −2.3 |
| 1–39                                          | 2921  | 19.2 | 36  | 16.3 | −7.5  | 2915  | 19.1 | 42  | 19.1 | 0.4  |
| ≥40                                           | 3485  | 22.9 | 54  | 24.4 | 3.7   | 3489  | 22.9 | 52  | 23.6 | 2.0  |
| Missing                                       | 1868  | 12.3 | 25  | 11.3 | −2.9  | 1866  | 12.2 | 27  | 12.3 | 0.4  |
| ADL on admission (Barthel index score)        |       |      |     |      |       |       |      |     |      |      |
| 100                                           | 4349  | 28.5 | 65  | 29.4 | 1.9   | 4351  | 28.5 | 61  | 27.7 | −2.3 |
| ≤95                                           | 8089  | 53.1 | 130 | 58.8 | 11.6  | 8102  | 53.2 | 122 | 55.5 | 4.1  |
| Missing                                       | 2802  | 18.4 | 26  | 11.8 | −18.6 | 2788  | 18.3 | 38  | 17.3 | −2.7 |
| Frequency of hospitalization before admission |       |      |     |      |       |       |      |     |      |      |
| 0                                             | 8839  | 58.0 | 121 | 54.8 | −6.6  | 8832  | 57.9 | 119 | 54.1 | −7.6 |
| 1–2                                           | 4631  | 30.4 | 66  | 29.9 | −1.1  | 4630  | 30.4 | 70  | 31.8 | 3.4  |
| ≥ 3                                           | 1770  | 11.6 | 34  | 15.4 | 11.1  | 1778  | 11.7 | 31  | 14.1 | 6.6  |
| Academic hospital                             | 12333 | 80.9 | 159 | 71.9 | −21.2 | 12314 | 80.8 | 180 | 81.8 | 2.4  |

|                             |       |      |     |      |       |       |      |     |      |      |
|-----------------------------|-------|------|-----|------|-------|-------|------|-----|------|------|
| Unscheduled hospitalization | 12122 | 79.5 | 178 | 80.5 | 2.5   | 12125 | 79.6 | 172 | 78.2 | −3.6 |
| Emergency ward admission    | 1704  | 11.2 | 14  | 6.3  | −17.2 | 1694  | 11.1 | 28  | 12.7 | 6.1  |
| ICU admission               | 866   | 5.7  | 14  | 6.3  | 2.7   | 867   | 5.7  | 16  | 7.3  | 7.3  |

Data are presented as n (%).

BMI, body mass index; ADL, activities of daily living; ICU, intensive care unit; IPTW, inverse probability of treatment weighting; SMD, standardized mean difference

**Table S3.** Comorbidities and treatments before and after stabilized IPTW using propensity scores in the sensitivity analyses 1

| Variables                                     | All patients                               |      |                                         |      |       | Patients after IPTW estimation             |      |                                         |      |       |
|-----------------------------------------------|--------------------------------------------|------|-----------------------------------------|------|-------|--------------------------------------------|------|-----------------------------------------|------|-------|
|                                               | High-dose corticosteroid group (n = 15240) | %    | Low-dose corticosteroid group (n = 221) | %    | SMD   | High-dose corticosteroid group (n = 15241) | %    | Low-dose corticosteroid group (n = 220) | %    | SMD   |
| Comorbidity                                   |                                            |      |                                         |      |       |                                            |      |                                         |      |       |
| Pneumonia                                     | 2493                                       | 16.4 | 44                                      | 19.9 | 9.2   | 2501                                       | 16.4 | 37                                      | 16.8 | 1.3   |
| Mycotic infection                             | 177                                        | 1.2  | 3                                       | 1.4  | 1.8   | 177                                        | 1.2  | 2                                       | 0.9  | -1.1  |
| Pulmonary embolism                            | 81                                         | 0.5  | 0                                       | 0.0  | -10.3 | 81                                         | 0.5  | 0                                       | 0.0  | -10.3 |
| Bronchiectasis                                | 603                                        | 4.0  | 14                                      | 6.3  | 10.8  | 608                                        | 4.0  | 5                                       | 2.3  | -7.5  |
| Pneumothorax                                  | 102                                        | 0.7  | 5                                       | 2.3  | 13.3  | 105                                        | 0.7  | 1                                       | 0.5  | -2.3  |
| Cor pulmonale                                 | 130                                        | 0.9  | 4                                       | 1.8  | 8.3   | 132                                        | 0.9  | 3                                       | 1.4  | 3.9   |
| Lung cancer                                   | 1774                                       | 11.6 | 28                                      | 12.7 | 3.1   | 1776                                       | 11.7 | 33                                      | 15.0 | 10.9  |
| Other types of cancer*                        | 1514                                       | 9.9  | 22                                      | 10.0 | 0.1   | 1514                                       | 9.9  | 24                                      | 10.9 | 2.5   |
| Disseminated intravascular coagulation        | 985                                        | 6.5  | 18                                      | 8.1  | 6.5   | 989                                        | 6.5  | 14                                      | 6.4  | -0.9  |
| Chronic heart failure                         | 1581                                       | 10.4 | 21                                      | 9.5  | -2.9  | 1579                                       | 10.4 | 22                                      | 10.0 | -0.6  |
| Tachycardia                                   | 742                                        | 4.9  | 13                                      | 5.9  | 4.5   | 744                                        | 4.9  | 14                                      | 6.4  | 5.8   |
| Acute coronary syndrome                       | 1001                                       | 6.6  | 19                                      | 8.6  | 7.7   | 1006                                       | 6.6  | 17                                      | 7.7  | 4.3   |
| Diabetes mellitus                             | 3823                                       | 25.1 | 62                                      | 28.1 | 6.7   | 3830                                       | 25.1 | 70                                      | 31.8 | 15.5  |
| Stroke                                        | 818                                        | 5.4  | 19                                      | 8.6  | 12.7  | 825                                        | 5.4  | 10                                      | 4.5  | -3.5  |
| Dementia                                      | 386                                        | 2.5  | 9                                       | 4.1  | 8.6   | 389                                        | 2.6  | 6                                       | 2.7  | 0.1   |
| Renal failure                                 | 851                                        | 5.6  | 13                                      | 5.9  | 1.3   | 852                                        | 5.6  | 13                                      | 5.9  | 2.2   |
| Liver dysfunction                             | 724                                        | 4.8  | 13                                      | 5.9  | 5.0   | 727                                        | 4.8  | 10                                      | 4.5  | -0.8  |
| Gastroesophageal reflux disease               | 2938                                       | 19.3 | 25                                      | 11.3 | -22.2 | 2921                                       | 19.2 | 43                                      | 19.5 | 0.7   |
| Treatment within 3 days after hospitalization |                                            |      |                                         |      |       |                                            |      |                                         |      |       |
| Noradrenaline                                 | 497                                        | 3.3  | 11                                      | 5.0  | 8.6   | 501                                        | 3.3  | 13                                      | 5.9  | 13.3  |

|                                           |      |      |    |      |       |      |      |    |      |      |
|-------------------------------------------|------|------|----|------|-------|------|------|----|------|------|
| Azithromycin                              | 2087 | 13.7 | 12 | 5.4  | −28.4 | 2069 | 13.6 | 31 | 14.1 | 2.4  |
| Cyclophosphamide<br>(intravenous)         | 199  | 1.3  | 1  | 0.5  | −9.1  | 197  | 1.3  | 2  | 0.9  | −3.6 |
| Cyclosporin                               | 414  | 2.7  | 5  | 2.3  | −2.9  | 413  | 2.7  | 8  | 3.6  | 4.9  |
| Tacrolimus                                | 77   | 0.5  | 2  | 0.9  | 4.8   | 78   | 0.5  | 1  | 0.5  | −3.2 |
| Azathioprine                              | 73   | 0.5  | 1  | 0.5  | −0.4  | 73   | 0.5  | 1  | 0.5  | −1.0 |
| Pirfenidone                               | 249  | 1.6  | 3  | 1.4  | −2.3  | 248  | 1.6  | 3  | 1.4  | −2.0 |
| Nintedanib                                | 98   | 0.6  | 1  | 0.5  | −2.6  | 98   | 0.6  | 0  | 0.0  | −5.9 |
| Sivelestat sodium hydrate                 | 1406 | 9.2  | 8  | 3.6  | −23.0 | 1394 | 9.1  | 18 | 8.2  | −4.0 |
| Thrombomodulin alfa                       | 399  | 2.6  | 5  | 2.3  | −2.3  | 398  | 2.6  | 4  | 1.8  | −5.9 |
| Mechanical ventilation                    | 2576 | 16.9 | 31 | 14.0 | −8.0  | 2570 | 16.9 | 42 | 19.1 | 6.1  |
| Hemodialysis                              | 219  | 1.4  | 2  | 0.9  | −4.9  | 218  | 1.4  | 4  | 1.8  | 2.0  |
| High-flow nasal<br>cannula oxygen therapy | 518  | 3.4  | 4  | 1.8  | −10.0 | 515  | 3.4  | 5  | 2.3  | −5.6 |
| Transfusion                               | 304  | 2.0  | 13 | 5.9  | 20.1  | 313  | 2.1  | 4  | 1.8  | −0.2 |
| Enteral tube feeding                      | 502  | 3.3  | 8  | 3.6  | 1.8   | 502  | 3.3  | 12 | 5.5  | 10.9 |

Data are presented as n (%).

IPTW, inverse probability of treatment weighting; SMD, standardized mean difference

\*Detailed information in Table S1.

**Table S4.** Outcomes of sensitivity analyses 1 in the high- and low-dose corticosteroid groups before and after stabilized IPTW

|                                               | Patients before IPTW estimation |                               | Patients after IPTW estimation |                               |
|-----------------------------------------------|---------------------------------|-------------------------------|--------------------------------|-------------------------------|
|                                               | High-dose corticosteroid group  | Low-dose corticosteroid group | High-dose corticosteroid group | Low-dose corticosteroid group |
| All patients, (n)                             | 15240                           | 221                           | 15241                          | 220                           |
| In-hospital mortality, n (%)                  | 7841 (51.5)                     | 116 (52.5)                    | 7847 (51.5)                    | 105 (47.7)                    |
| 28-day mortality, n (%)                       | 5037 (33.1)                     | 71 (32.1)                     | 5039 (33.1)                    | 65 (29.5)                     |
| Infection during hospitalization, n (%)       | 926 (6.1)                       | 18 (8.1)                      | 927 (6.1)                      | 23 (10.5)                     |
| Length of hospital stay (days), median (IQR)  | 25 (15–42)                      | 25 (17–45)                    | 25 (15–42)                     | 25 (16–44)                    |
| Duration of steroid use (days), median (IQR)* | 23 (13–40)                      | 21 (12–41)                    | 23 (13–40)                     | 20 (12–40)                    |
| Discharge to home, n (%)                      | 5374 (35.3)                     | 73 (33.0)                     | 5367 (35.2)                    | 78 (35.5)                     |
| Survivors, (n)                                | 7399                            | 105                           | 7394                           | 116                           |
| Infection during hospitalization, n (%)       | 284 (3.8)                       | 7 (6.7)                       | 284 (3.8)                      | 9 (7.8)                       |
| Length of hospital stay (days), median (IQR)  | 30 (19–46)                      | 29 (18–48)                    | 30 (19–46)                     | 25 (16–47)                    |
| Duration of steroid use (days), median (IQR)* | 28 (16–43)                      | 23 (10–45)                    | 28 (16–43)                     | 21 (10–44)                    |

IPTW, inverse probability of treatment weighting; IQR, interquartile range

\*Steroids include methylprednisolone and prednisolone.

**Table S5.** Comparison of outcomes between the high- and low-dose corticosteroid groups before and after stabilized IPTW in the sensitivity analyses 1

| Logistic regression analyses for patients in the low-dose corticosteroid group compared with the high-dose corticosteroid group                            |                        |           |         |                       |           |         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------|---------|-----------------------|-----------|---------|
|                                                                                                                                                            | Before IPTW estimation |           |         | After IPTW estimation |           |         |
|                                                                                                                                                            | Odds ratio             | 95% CI    | p value | Odds ratio            | 95% CI    | p value |
| All patients                                                                                                                                               |                        |           |         |                       |           |         |
| In-hospital mortality                                                                                                                                      | 1.04                   | 0.78–1.39 | 0.78    | 0.85                  | 0.60–1.20 | 0.36    |
| 28-day mortality                                                                                                                                           | 0.96                   | 0.72–1.28 | 0.78    | 0.85                  | 0.59–1.24 | 0.41    |
| Infection during hospitalization                                                                                                                           | 1.37                   | 0.87–2.17 | 0.18    | 1.79                  | 0.97–3.29 | 0.06    |
| Survivors                                                                                                                                                  |                        |           |         |                       |           |         |
| Infection during hospitalization                                                                                                                           | 1.79                   | 0.81–3.93 | 0.15    | 2.05                  | 0.69–6.13 | 0.20    |
| Incidence rate ratios of length of hospital stay and duration of steroid use in low-dose corticosteroid group compared with high-dose corticosteroid group |                        |           |         |                       |           |         |
|                                                                                                                                                            | Before IPTW estimation |           |         | After IPTW estimation |           |         |
|                                                                                                                                                            | Incidence rate ratio   | 95% CI    | p value | Incidence rate ratio  | 95% CI    | p value |
| All patients                                                                                                                                               |                        |           |         |                       |           |         |
| Length of hospital stay                                                                                                                                    | 1.01                   | 0.90–1.14 | 0.81    | 0.99                  | 0.86–1.14 | 0.90    |
| Duration of steroid use*                                                                                                                                   | 0.97                   | 0.85–1.10 | 0.63    | 0.96                  | 0.82–1.12 | 0.60    |
| Survivors                                                                                                                                                  |                        |           |         |                       |           |         |
| Length of hospital stay                                                                                                                                    | 1.05                   | 0.87–1.28 | 0.60    | 1.00                  | 0.80–1.25 | 0.97    |
| Duration of steroid use*                                                                                                                                   | 1.02                   | 0.81–1.27 | 0.89    | 0.98                  | 0.75–1.26 | 0.85    |

IPTW, inverse probability of treatment weighting; CI, confidence interval

\*Steroids include methylprednisolone and prednisolone.

**Table S6.** Baseline characteristics of patients before and after stabilized IPTW using propensity scores in the sensitivity analyses 2

| Characteristics                       | All patients                               |      |                                         |      |       | Patients after IPTW estimation             |      |                                         |      |       |
|---------------------------------------|--------------------------------------------|------|-----------------------------------------|------|-------|--------------------------------------------|------|-----------------------------------------|------|-------|
|                                       | High-dose corticosteroid group (n = 16539) | %    | Low-dose corticosteroid group (n = 293) | %    | SMD   | High-dose corticosteroid group (n = 16539) | %    | Low-dose corticosteroid group (n = 290) | %    | SMD   |
| Male sex                              | 11628                                      | 70.3 | 213                                     | 72.7 | 5.3   | 11635                                      | 70.4 | 206                                     | 71.0 | 1.3   |
| Age, years                            |                                            |      |                                         |      |       |                                            |      |                                         |      |       |
| 15–70                                 | 4602                                       | 27.8 | 74                                      | 25.3 | −5.8  | 4595                                       | 27.8 | 77                                      | 26.4 | −3.2  |
| 71–80                                 | 6785                                       | 41.0 | 105                                     | 35.8 | −10.7 | 6771                                       | 40.9 | 137                                     | 47.1 | 12.3  |
| ≥80                                   | 5040                                       | 30.5 | 111                                     | 37.9 | 15.7  | 5061                                       | 30.6 | 76                                      | 26.1 | −10.0 |
| Missing                               | 112                                        | 0.7  | 3                                       | 1.0  | 3.8   | 113                                        | 0.7  | 1                                       | 0.5  | −2.5  |
| Treatment year                        |                                            |      |                                         |      |       |                                            |      |                                         |      |       |
| 2010–2011                             | 2664                                       | 16.1 | 40                                      | 13.7 | −6.9  | 2657                                       | 16.1 | 47                                      | 16.3 | 0.7   |
| 2012–2013                             | 3671                                       | 22.2 | 59                                      | 20.1 | −5.0  | 3665                                       | 22.2 | 62                                      | 21.4 | −2.0  |
| 2014–2015                             | 4605                                       | 27.8 | 83                                      | 28.3 | 1.1   | 4606                                       | 27.9 | 76                                      | 26.3 | −3.6  |
| 2016–2017                             | 5599                                       | 33.9 | 111                                     | 37.9 | 8.4   | 5611                                       | 33.9 | 105                                     | 36.1 | 4.5   |
| BMI (kg/m <sup>2</sup> )              |                                            |      |                                         |      |       |                                            |      |                                         |      |       |
| <23                                   | 8613                                       | 52.1 | 164                                     | 56.0 | 7.8   | 8624                                       | 52.1 | 147                                     | 50.6 | −3.2  |
| 23–25                                 | 2988                                       | 18.1 | 47                                      | 16.0 | −5.4  | 2982                                       | 18.0 | 61                                      | 21.0 | 7.5   |
| ≥25                                   | 3115                                       | 18.8 | 57                                      | 19.5 | 1.6   | 3117                                       | 18.8 | 54                                      | 18.7 | −0.3  |
| Missing                               | 1823                                       | 11.0 | 25                                      | 8.5  | −8.4  | 1816                                       | 11.0 | 28                                      | 9.8  | −4.0  |
| Hugh–Jones dyspnea score on admission |                                            |      |                                         |      |       |                                            |      |                                         |      |       |
| 1–2                                   | 2089                                       | 12.6 | 35                                      | 11.9 | −2.1  | 2087                                       | 12.6 | 35                                      | 12.0 | −2.0  |
| 3                                     | 1336                                       | 8.1  | 22                                      | 7.5  | −2.1  | 1334                                       | 8.1  | 25                                      | 8.5  | 1.5   |
| 4                                     | 3011                                       | 18.2 | 51                                      | 17.4 | −2.1  | 3009                                       | 18.2 | 65                                      | 22.5 | 10.6  |
| 5                                     | 6608                                       | 40.0 | 117                                     | 39.9 | 0     | 6608                                       | 40.0 | 95                                      | 32.6 | −15.0 |
| Missing                               | 3495                                       | 21.1 | 68                                      | 23.2 | 5.0   | 3502                                       | 21.2 | 71                                      | 24.5 | 7.9   |

|                                               |       |      |     |      |       |       |      |     |      |      |
|-----------------------------------------------|-------|------|-----|------|-------|-------|------|-----|------|------|
| Japan Coma Scale score on admission           |       |      |     |      |       |       |      |     |      |      |
| 0- or 1-digit (alert or dull)                 | 16107 | 97.4 | 281 | 95.9 | −8.2  | 16103 | 97.4 | 282 | 97.4 | −0.5 |
| 2-digit (somnolence)                          | 241   | 1.5  | 3   | 1.0  | −3.9  | 240   | 1.4  | 4   | 1.3  | −1.3 |
| 3-digit (coma)                                | 191   | 1.2  | 9   | 3.1  | 13.4  | 197   | 1.2  | 4   | 1.4  | 2.0  |
| Charlson comorbidity index                    |       |      |     |      |       |       |      |     |      |      |
| 0                                             | 8548  | 51.7 | 104 | 35.5 | −33.1 | 8502  | 51.4 | 160 | 55.2 | 7.6  |
| 1                                             | 2157  | 13.0 | 86  | 29.4 | 40.7  | 2204  | 13.3 | 36  | 12.2 | −3.3 |
| 2                                             | 3569  | 21.6 | 56  | 19.1 | −6.1  | 3562  | 21.5 | 54  | 18.6 | −7.3 |
| ≥3                                            | 2265  | 13.7 | 47  | 16.0 | 6.6   | 2272  | 13.7 | 41  | 14.0 | 0.7  |
| Smoking index, pack-years                     |       |      |     |      |       |       |      |     |      |      |
| 0                                             | 7395  | 44.7 | 129 | 44.0 | −1.4  | 7393  | 44.7 | 129 | 44.4 | −0.7 |
| 1–39                                          | 3167  | 19.1 | 49  | 16.7 | −6.3  | 3160  | 19.1 | 54  | 18.7 | −1.1 |
| ≥40                                           | 3964  | 24.0 | 83  | 28.3 | 9.9   | 3977  | 24.0 | 70  | 24.3 | 0.5  |
| Missing                                       | 2013  | 12.2 | 32  | 10.9 | −3.9  | 2009  | 12.2 | 37  | 12.7 | 1.7  |
| ADL on admission (Barthel index score)        |       |      |     |      |       |       |      |     |      |      |
| 100                                           | 4709  | 28.5 | 84  | 28.7 | 0.4   | 4710  | 28.5 | 86  | 29.5 | 2.3  |
| ≤95                                           | 8804  | 53.2 | 176 | 60.1 | 13.8  | 8824  | 53.4 | 156 | 53.9 | 1.0  |
| Missing                                       | 3026  | 18.3 | 33  | 11.3 | −19.9 | 3006  | 18.2 | 48  | 16.7 | −4.0 |
| Frequency of hospitalization before admission |       |      |     |      |       |       |      |     |      |      |
| 0                                             | 9458  | 57.2 | 161 | 54.9 | −4.5  | 9452  | 57.1 | 154 | 53.2 | −8.0 |
| 1–2                                           | 5094  | 30.8 | 85  | 29.0 | −3.9  | 5089  | 30.8 | 100 | 34.4 | 7.7  |
| ≥ 3                                           | 1987  | 12.0 | 47  | 16.0 | 11.6  | 1998  | 12.1 | 36  | 12.4 | 1.1  |
| Academic hospital                             | 13328 | 80.6 | 218 | 74.4 | −14.8 | 13310 | 80.5 | 234 | 80.7 | 0.4  |

|                             |       |      |     |      |       |       |      |     |      |      |
|-----------------------------|-------|------|-----|------|-------|-------|------|-----|------|------|
| Unscheduled hospitalization | 13189 | 79.7 | 237 | 80.9 | 2.9   | 13192 | 79.8 | 228 | 78.5 | −3.4 |
| Emergency ward admission    | 1833  | 11.1 | 20  | 6.8  | −14.9 | 1821  | 11.0 | 34  | 11.7 | 2.3  |
| ICU admission               | 938   | 5.7  | 15  | 5.1  | −2.4  | 937   | 5.7  | 22  | 7.5  | 8.0  |

Data are presented as n (%).

BMI, body mass index; ADL, activities of daily living; ICU, intensive care unit; IPTW, inverse probability of treatment weighting; SMD, standardized mean difference

**Table S7.** Comorbidities and treatments before and after stabilized IPTW using propensity scores in the sensitivity analyses 2

| Variables                              | All patients                               |      |                                         |      |       | Patients after IPTW estimation             |      |                                         |      |      |
|----------------------------------------|--------------------------------------------|------|-----------------------------------------|------|-------|--------------------------------------------|------|-----------------------------------------|------|------|
|                                        | High-dose corticosteroid group (n = 16539) | %    | Low-dose corticosteroid group (n = 293) | %    | SMD   | High-dose corticosteroid group (n = 16539) | %    | Low-dose corticosteroid group (n = 290) | %    | SMD  |
| Comorbidity                            |                                            |      |                                         |      |       |                                            |      |                                         |      |      |
| Bronchial asthma                       | 983                                        | 5.9  | 47                                      | 16.0 | 32.7  | 1012                                       | 6.1  | 18                                      | 6.0  | -0.3 |
| COPD                                   | 805                                        | 4.9  | 47                                      | 16.0 | 37.1  | 838                                        | 5.1  | 15                                      | 5.0  | -0.2 |
| Pneumonia                              | 2666                                       | 16.1 | 56                                      | 19.1 | 7.9   | 2675                                       | 16.2 | 47                                      | 16.2 | 0    |
| Mycotic infection                      | 189                                        | 1.1  | 4                                       | 1.4  | 2.0   | 190                                        | 1.1  | 4                                       | 1.3  | 1.5  |
| Pulmonary embolism                     | 89                                         | 0.5  | 1                                       | 0.3  | -3.0  | 88                                         | 0.5  | 0                                       | 0.1  | -5.9 |
| Bronchiectasis                         | 696                                        | 4.2  | 15                                      | 5.1  | 4.3   | 698                                        | 4.2  | 8                                       | 2.7  | -7.2 |
| Pneumothorax                           | 109                                        | 0.7  | 6                                       | 2.0  | 12.0  | 113                                        | 0.7  | 1                                       | 0.5  | -1.8 |
| Cor pulmonale                          | 151                                        | 0.9  | 5                                       | 1.7  | 7.0   | 154                                        | 0.9  | 5                                       | 1.7  | 6.6  |
| Lung cancer                            | 1992                                       | 12.0 | 41                                      | 14.0 | 5.8   | 1997                                       | 12.1 | 35                                      | 12.0 | -0.1 |
| Other types of cancer*                 | 1586                                       | 9.6  | 25                                      | 8.5  | -3.7  | 1583                                       | 9.6  | 27                                      | 9.4  | -0.5 |
| Disseminated intravascular coagulation | 1059                                       | 6.4  | 20                                      | 6.8  | 1.7   | 1060                                       | 6.4  | 18                                      | 6.2  | -0.7 |
| Chronic heart failure                  | 1735                                       | 10.5 | 37                                      | 12.6 | 6.7   | 1741                                       | 10.5 | 27                                      | 9.3  | -3.8 |
| Tachycardia                            | 789                                        | 4.8  | 12                                      | 4.1  | -3.3  | 787                                        | 4.8  | 23                                      | 7.9  | 15.0 |
| Acute coronary syndrome                | 1082                                       | 6.5  | 22                                      | 7.5  | 3.8   | 1085                                       | 6.6  | 23                                      | 8.1  | 5.8  |
| Diabetes mellitus                      | 4168                                       | 25.2 | 80                                      | 27.3 | 4.8   | 4175                                       | 25.2 | 87                                      | 30.1 | 10.9 |
| Stroke                                 | 873                                        | 5.3  | 21                                      | 7.2  | 7.8   | 879                                        | 5.3  | 15                                      | 5.3  | 0.1  |
| Dementia                               | 417                                        | 2.5  | 8                                       | 2.7  | 1.3   | 418                                        | 2.5  | 8                                       | 2.8  | 1.6  |
| Renal failure                          | 910                                        | 5.5  | 13                                      | 4.4  | -4.9  | 907                                        | 5.5  | 17                                      | 5.9  | 1.7  |
| Liver dysfunction                      | 767                                        | 4.6  | 16                                      | 5.5  | 3.8   | 769                                        | 4.7  | 13                                      | 4.6  | -0.1 |
| Gastroesophageal reflux disease        | 3281                                       | 19.8 | 42                                      | 14.3 | -14.6 | 3265                                       | 19.7 | 53                                      | 18.4 | -3.6 |

|                                                  |      |      |    |      |       |      |      |    |      |      |
|--------------------------------------------------|------|------|----|------|-------|------|------|----|------|------|
| Treatment within 3 days<br>after hospitalization |      |      |    |      |       |      |      |    |      |      |
| Noradrenaline                                    | 519  | 3.1  | 16 | 5.5  | 11.5  | 526  | 3.2  | 17 | 6.0  | 13.9 |
| Azithromycin                                     | 2253 | 13.6 | 21 | 7.2  | -21.3 | 2234 | 13.5 | 36 | 12.3 | -4.0 |
| Cyclophosphamide<br>(intravenous)                | 213  | 1.3  | 1  | 0.3  | -10.5 | 210  | 1.3  | 3  | 0.9  | -3.9 |
| Cyclosporin                                      | 463  | 2.8  | 5  | 1.7  | -7.4  | 460  | 2.8  | 10 | 3.5  | 5.1  |
| Tacrolimus                                       | 81   | 0.5  | 3  | 1.0  | 6.2   | 83   | 0.5  | 1  | 0.3  | -2.4 |
| Azathioprine                                     | 78   | 0.5  | 2  | 0.7  | 2.8   | 79   | 0.5  | 1  | 0.3  | -2.4 |
| Pirfenidone                                      | 297  | 1.8  | 4  | 1.4  | -3.5  | 296  | 1.8  | 6  | 2.0  | 1.7  |
| Nintedanib                                       | 112  | 0.7  | 1  | 0.3  | -4.7  | 111  | 0.7  | 1  | 0.4  | -3.8 |
| Sivelestat sodium hydrate                        | 1529 | 9.2  | 9  | 3.1  | -25.9 | 1511 | 9.1  | 24 | 8.2  | -3.8 |
| Thrombomodulin alfa                              | 428  | 2.6  | 6  | 2.0  | -3.6  | 427  | 2.6  | 5  | 1.6  | -6.3 |
| Mechanical ventilation                           | 2766 | 16.7 | 35 | 11.9 | -13.7 | 2753 | 16.6 | 53 | 18.2 | 4.3  |
| Hemodialysis                                     | 228  | 1.4  | 2  | 0.7  | -6.9  | 226  | 1.4  | 4  | 1.3  | -0.3 |
| High-flow nasal<br>cannula oxygen therapy        | 566  | 3.4  | 7  | 2.4  | -6.1  | 563  | 3.4  | 8  | 2.7  | -4.5 |
| Transfusion                                      | 315  | 1.9  | 11 | 3.8  | 11.2  | 321  | 1.9  | 7  | 2.6  | 3.8  |
| Enteral tube feeding                             | 533  | 3.2  | 9  | 3.1  | -0.9  | 533  | 3.2  | 16 | 5.3  | 12.1 |

Data are presented as n (%).

COPD, chronic obstructive pulmonary disease; IPTW, inverse probability of treatment weighting; SMD, standardized mean difference

\*Detailed information in Table S1.

**Table S8.** Outcomes of sensitivity analyses 2 in the high- and low-dose corticosteroid groups before and after stabilized IPTW

|                                               | Patients before IPTW estimation |                               | Patients after IPTW estimation |                               |
|-----------------------------------------------|---------------------------------|-------------------------------|--------------------------------|-------------------------------|
|                                               | High-dose corticosteroid group  | Low-dose corticosteroid group | High-dose corticosteroid group | Low-dose corticosteroid group |
| All patients, (n)                             | 16539                           | 293                           | 16539                          | 290                           |
| In-hospital mortality, n (%)                  | 8491 (51.3)                     | 146 (49.8)                    | 8493 (51.4)                    | 135 (46.6)                    |
| 28-day mortality, n (%)                       | 5401 (32.7)                     | 85 (29.0)                     | 5398 (32.6)                    | 86 (29.7)                     |
| Infection during hospitalization, n (%)       | 998 (6.0)                       | 24 (8.2)                      | 998 (6.0)                      | 30 (10.3)                     |
| Length of hospital stay (days), median (IQR)  | 26 (16–43)                      | 26 (16–45)                    | 26 (16–43)                     | 25 (16–44)                    |
| Duration of steroid use (days), median (IQR)* | 23 (13–40)                      | 21 (12–40)                    | 23 (13–40)                     | 21 (12–40)                    |
| Discharge to home, n (%)                      | 5860 (35.4)                     | 102 (34.8)                    | 5857 (35.4)                    | 108 (37.2)                    |
| Survivors, (n)                                | 8048                            | 147                           | 8046                           | 155                           |
| Infection during hospitalization, n (%)       | 314 (3.9)                       | 9 (6.1)                       | 314 (3.9)                      | 11 (7.1)                      |
| Length of hospital stay (days), median (IQR)  | 30 (19–46)                      | 28 (16–48)                    | 30 (19–46)                     | 29 (16–48)                    |
| Duration of steroid use (days), median (IQR)* | 28 (16–44)                      | 22 (9–44)                     | 28 (16–44)                     | 22 (10–45)                    |

IPTW, inverse probability of treatment weighting; IQR, interquartile range

\*Steroids include methylprednisolone and prednisolone.

**Table S9.** Comparison of outcomes between the high- and low-dose corticosteroid groups before and after stabilized IPTW in the sensitivity analyses 2

| Logistic regression analyses for patients in the low-dose corticosteroid group compared with the high-dose corticosteroid group                            |                        |           |         |                       |           |         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------|---------|-----------------------|-----------|---------|
|                                                                                                                                                            | Before IPTW estimation |           |         | After IPTW estimation |           |         |
|                                                                                                                                                            | Odds ratio             | 95% CI    | p value | Odds ratio            | 95% CI    | p value |
| All patients                                                                                                                                               |                        |           |         |                       |           |         |
| In-hospital mortality                                                                                                                                      | 0.94                   | 0.73–1.21 | 0.64    | 0.82                  | 0.60–1.12 | 0.22    |
| 28-day mortality                                                                                                                                           | 0.83                   | 0.65–1.09 | 0.20    | 0.86                  | 0.62–1.21 | 0.39    |
| Infection during hospitalization                                                                                                                           | 1.39                   | 0.93–2.08 | 0.11    | 1.79                  | 0.97–3.10 | 0.06    |
| Survivors                                                                                                                                                  |                        |           |         |                       |           |         |
| Infection during hospitalization                                                                                                                           | 1.61                   | 0.80–3.23 | 0.18    | 1.96                  | 0.70–5.43 | 0.20    |
| Incidence rate ratios of length of hospital stay and duration of steroid use in low-dose corticosteroid group compared with high-dose corticosteroid group |                        |           |         |                       |           |         |
|                                                                                                                                                            | Before IPTW estimation |           |         | After IPTW estimation |           |         |
|                                                                                                                                                            | Incidence rate ratio   | 95% CI    | p value | Incidence rate ratio  | 95% CI    | p value |
| All patients                                                                                                                                               |                        |           |         |                       |           |         |
| Length of hospital stay                                                                                                                                    | 1.02                   | 0.92–1.13 | 0.72    | 1.02                  | 0.86–1.21 | 0.84    |
| Duration of steroid use*                                                                                                                                   | 0.96                   | 0.85–1.09 | 0.56    | 0.99                  | 0.81–1.20 | 0.89    |
| Survivors                                                                                                                                                  |                        |           |         |                       |           |         |
| Length of hospital stay                                                                                                                                    | 1.02                   | 0.87–1.19 | 0.80    | 1.08                  | 0.83–1.40 | 0.58    |
| Duration of steroid use*                                                                                                                                   | 0.96                   | 0.79–1.15 | 0.63    | 1.05                  | 0.77–1.41 | 0.77    |

IPTW, inverse probability of treatment weighting; CI, confidence interval

\*Steroids include methylprednisolone and prednisolone.