

## Supplementary Table 1

### *Concomitant respiratory medications during the in-hospital phase*

| Drug class                                 | All            | Metformin      | Placebo       | P-value |
|--------------------------------------------|----------------|----------------|---------------|---------|
| <b>Inhaled/nebulised therapy</b>           | <b>(n=51*)</b> | <b>(n=33*)</b> | <b>(n=18)</b> |         |
| Short-acting $\beta$ -agonist              | 49 (96%)       | 31 (94%)       | 18 (100%)     | 0.287   |
| Short-acting antimuscarinic                | 37 (73%)       | 23 (70%)       | 14 (78%)      | 0.537   |
| Long-acting $\beta$ -agonist (without ICS) | 3 (6%)         | 2 (6%)         | 1 (6%)        | 0.942   |
| Long-acting antimuscarinic                 | 27 (53%)       | 19 (58%)       | 8 (44%)       | 0.369   |
| ICS-LABA combination                       | 46 (90%)       | 30 (91%)       | 16 (89%)      | 0.817   |
| <b>Systemic therapy</b>                    | <b>(n=49†)</b> | <b>(n=31†)</b> | <b>(n=18)</b> |         |
| Systemic corticosteroid                    | 48 (98%)       | 30 (97%)       | 18 (100%)     | 0.441   |
| Antibiotic                                 | 43 (88%)       | 29 (94%)       | 14 (78%)      | 0.105   |
| Methylxanthine                             | 17 (35%)       | 8 (26%)        | 9 (50%)       | 0.086   |
| Mucolytic                                  | 37 (76%)       | 22 (71%)       | 15 (83%)      | 0.332   |
| Leukotriene receptor antagonist            | 1 (2%)         | 1 (3%)         | 0 (0%)        | 0.441   |
| Magnesium                                  | 1 (2%)         | 0 (0%)         | 1 (6%)        | 0.185   |

ICS, inhaled corticosteroid; LABA, long-acting  $\beta$ -agonist.

\* Records of inhaled/nebulised medications were not available for one participant

† Records of acute systemic respiratory medications were not available for three participants

## Supplementary Table 2

### *Characteristics of the study groups with respect to severity of airflow limitation*

| Characteristic*                          | Summary metric*            | All (n=52) | Metformin (n=34) | Placebo (n=18) | P-value |
|------------------------------------------|----------------------------|------------|------------------|----------------|---------|
| <b>Spirometry not completed</b>          | <i>n (%)</i>               | 9 (17%)    | 7 (21%)          | 2 (11%)        | 0.470   |
| <b>FEV<sub>1</sub>:FVC ratio ≥0.7</b>    | <i>n (%<sup>ii</sup>)</i>  | 5 (12%)    | 4 (15%)          | 1 (6%)         | 0.642   |
| <b>FEV<sub>1</sub>:FVC ratio &lt;0.7</b> | <i>n (%<sup>ii</sup>)</i>  | 38 (88%)   | 23 (85%)         | 15 (94%)       |         |
| GOLD 1 (≥80% predicted)                  | <i>n (%<sup>iii</sup>)</i> | 1 (3%)     | 0 (0%)           | 1 (7%)         | 0.677   |
| GOLD 2 (50–79% predicted)                | <i>n (%<sup>iii</sup>)</i> | 10 (26%)   | 6 (26%)          | 4 (27%)        |         |
| GOLD 3 (30–49% predicted)                | <i>n (%<sup>iii</sup>)</i> | 15 (39%)   | 10 (43%)         | 5 (33%)        |         |
| GOLD 4 (<30% predicted)                  | <i>n (%<sup>iii</sup>)</i> | 12 (32%)   | 7 (30%)          | 5 (33%)        |         |
| Best FEV <sub>1</sub> † — % predicted    | <i>mean±SD</i>             | 44±25      | 43±16            | 47±35          | 0.699   |

FEV<sub>1</sub>, forced expiratory volume in 1 second, expressed as a percentage of the predicted value; FVC, forced vital capacity; GOLD, Global initiative for chronic Obstructive Lung Disease; SD, standard deviation

\* The denominators for calculation of percentages are: *i.* all participants; *ii.* all participants who undertook spirometry; *iii.* all participants with obstructive spirometry (FEV<sub>1</sub>:FVC ratio <0.7)

† The 'best' FEV<sub>1</sub> is the highest value recorded from the valid spirometry attempts made at hospital discharge and 1-month follow-up, among patients with FEV<sub>1</sub>:FVC ratio <0.7.

### Supplementary Table 3

#### *Sensitivity analyses using alternative summary metrics of in-hospital blood*

#### *glucose concentration*

| Summary metric                                      | Mean ( $\pm$ SD)       |                      | Between-group difference (95% CI) | P-value |
|-----------------------------------------------------|------------------------|----------------------|-----------------------------------|---------|
|                                                     | Metformin group (n=34) | Placebo group (n=18) |                                   |         |
| Mean pre-breakfast glucose concentration (mmol/L)   | 5.0 $\pm$ 0.8          | 5.5 $\pm$ 2.3        | -0.6 (-1.4 to +0.3)               | 0.197   |
| Peak capillary blood glucose concentration (mmol/L) | 12.4 $\pm$ 3.3         | 12.4 $\pm$ 4.8       | 0.05 (-2.2 to +2.3)               | 0.966   |

SD, standard deviation; CI, confidence interval

## Supplementary Table 4

### *Sensitivity analysis using subgroups defined by baseline (day 1) blood glucose concentration*

| Subgroup                                                                                                                     | Mean $\pm$ SD        |                      | Between-group difference (95% CI) | P-value |
|------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|-----------------------------------|---------|
|                                                                                                                              | Metformin group      | Placebo group        |                                   |         |
| Participants with mean day 1 blood glucose concentration in lower 50 <sup>th</sup> centile                                   | 6.8 $\pm$ 0.6 (n=16) | 6.6 $\pm$ 0.6 (n=10) | -0.1 (-0.4 to +0.6)               | 0.604   |
| Participants with mean day 1 blood glucose concentration in upper 50 <sup>th</sup> centile                                   | 7.3 $\pm$ 1.0 (n=18) | 9.6 $\pm$ 4.6 (n=8)  | -2.3 (-6.1 to +1.5)               | 0.201   |
| Participants with mean day 1 blood glucose concentration in upper 50 <sup>th</sup> centile (excluding outlying observation*) | 7.3 $\pm$ 1.0 (n=18) | 8.1 $\pm$ 1.7 (n=7)  | -0.8 (-2.4 to +0.8)               | 0.166   |

SD, standard deviation; CI, confidence interval

\*Outlying observation in the placebo group with a mean blood glucose concentration more than 10 standard deviations from the overall cohort mean; see manuscript for further details.