

Supplementary Material

Article Title: Antipsychotic Use and Bloodstream Infections Among Adult Patients With Chronic Obstructive Pulmonary Disease: A Cohort Study

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Supplementary Table 1. Standardized differences of main characteristics after inverse probability weighting

| Baseline characteristic | SMD ^a |
|--------------------------|------------------|
| Age, years | 0.005 |
| Past hospital admissions | 0.006 |
| Cerebrovascular disease | 0.008 |
| Active malignancy | 0.001 |
| Diabetes mellitus | 0.002 |
| Dementia | 0.006 |
| Myocardial infarction | 0.001 |
| Inhaled corticosteroids | 0.001 |

a. Absolute values. SMD: Standardized mean differences between patients who were prescribed antipsychotics or benzodiazepines

Supplementary Table 2. Indications for new antipsychotic and benzodiazepine drugs users.

| Indications for antipsychotic or benzodiazepine drugs, no. (%) ^a | Entire cohort (n=923) | Antipsychotic use (n=366) | No antipsychotic use ^b (n=557) |
|---|-----------------------|---------------------------|---|
| Delirium - continued treatment after hospital discharge | 158 (17.1) | 123 (33.6) | 35 (6.3) |
| Dementia related psychosis or agitation | 77 (8.3) | 62 (17.0) | 15 (2.7) |
| Depressive and anxiety disorders | 259 (28.1) | 52 (14.3) | 207 (37.2) |
| Sleep-wake disorders | 182 (19.7) | 38 (10.4) | 144 (25.9) |

- a. Indications for prescription were identified by review of electronic medical charts when available. Indications for antipsychotic or benzodiazepine drugs were not exclusive (patients could present multiple indications for the same drug at the time of prescription).
b. Reference group comprised by benzodiazepine users.

Supplementary Table 3. Description of blood stream infections at one year of follow up

| Source of infection | Gram negative bacteremia (n=25) | Gram positive bacteremia (n=10) |
|---|---------------------------------|---------------------------------|
| Urinary tract infection | 11 | 1 |
| Lower respiratory tract infection | 5 | 5 |
| Intra-abdominal sepsis | 4 | 1 |
| Bacteremia with unclear source | 3 | 1 |
| Other source (bone, central nervous system) | 2 | 2 |

Supplementary Table 4. Summary of sensitivity analysis

| | Hazard ratio (95% CI) |
|--|-----------------------|
| Restricted to highly used antipsychotics (i.e., haloperidol, quetiapine, olanzapine, risperidone) ^a | 2.42 (1.10 - 5.33) |
| Excluding users of both benzodiazepine and antipsychotics during follow-up ^a | 1.72 (0.66 - 4.48) |
| Follow-up up to 5 years ^a | 1.65 (0.99 - 2.75) |
| Follow-up up to 30 days ^a | 1.86 (0.60 - 5.75) |
| Fine & Gray sub-distribution hazard model ^b | 2.31 (1.11 - 4.80) |
| Marginal structural Cox proportional model ^c | 2.30 (1.12 - 4.74) |
| Comparing pure D2 antagonists to sedative antipsychotics ^{a,d} | 5.20 (1.53 - 17.67) |
| Including the indication for antipsychotic or benzodiazepine drugs ^{a,e} | 1.41 (0.56 - 3.63) |

a. Cox proportional hazards model conditional on the propensity score, b. Sub-distribution hazard ratio to account for the competing risk of death

c. Inverse probability of treatment weighting using stabilized weights.

d. Pure D2 antagonists: risperidone and haloperidol. Sedative antipsychotics: mostly quetiapine and olanzapine based on local practice.

e. Indications for prescription were identified by review of electronic medical charts when available.

Abbreviations: CI: confidence interval