## Comparison of three cohorts of COVID-19 patients with different severity: exposure to antihypertensive, antidiabetic and lipid-lowering agents

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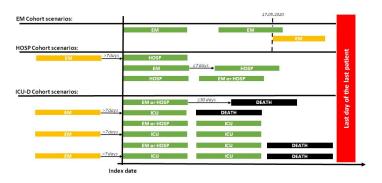
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## Abstract

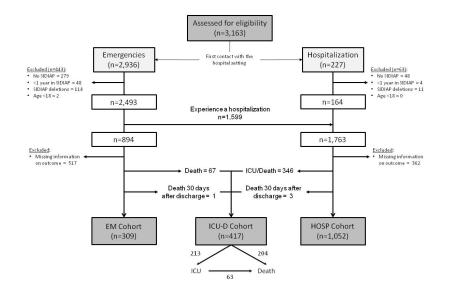
Aim: The association between COVID-19 disease severity and certain medicines for the treatment of chronic diseases is currently under discussion. We herein evaluated if previous exposure to antihypertensive, hypoglycaemic, and lipid-lowering drugs increases the risk of poorer COVID-19 outcomes. Methods: We performed a retrospective study on three cohorts of COVID-19 adult patients between March 2020 and May 2020 at the Vall d'Hebron University Hospital. Information relating to the patient lifestyle, comorbidities, and chronic exposures was retrieved from primary healthcare electronic records. Three cohorts were examined, namely patients who had died or required intensive care treatment (ICU/Death [ICU-D] Cohort), patients who required hospitalisation (Hospitalisation [HOSP] Cohort), and patients who only attended the emergency department (Emergencies [EM] Cohort). Descriptive statistics and a multivariate logistic regression model were used to investigate associations with drug exposure, where EM was employed as the reference cohort. Results: We included 1,778 patients: 417 (23.5%) from the ICU-D Cohort, 1,052 (59.2%) from the HOSP Cohort, and 309 (17.4%) from the EM Cohort. After multiple imputations and data adjustment by potential confounders, no statistically significant association was observed between the COVID-19 severity and the use of antihypertensives, hypoglycaemic agents, or lipid-lowering agents, with the exception of calcium channel blockers (CCB) (ICU-D Cohort: OR 2.23; CI 95% [1.03–4.83]; P = 0.042). Conclusions: Most results on lifestyle characteristics and comorbidities related to COVID-19 severity were in agreement with current knowledge, although some associated factors are nowadays a matter of controversy and further investigation is required.

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\*This figure aims to visually clarify the three cohorts based on different combinations of episodes experienced by the patient, and which were considered for defining the tudes takes. Each patient is assigned a cohort based on the version of the scenario considered, but it should be noted that the index date could be determined by a different episode han that of the versor tourne. Bach rectangle preparation any giologic economic the hospital exiting or dates. In rectangles are of equal taxe despite the fact that they may represent different durations. The spacing between rectangles is random with the exception of those indicated. For each ICU episode, a patient was registered as being hospitalized (e.g. green rectangles). Yellow rectangles are not considered as hospitalization episodes. The dashed line indicates the last date considered for the inclusion of an EMG episode.



| Medicines group             | OR     |   |          |          |          |     |     |   |          | CI 95%      | P value |
|-----------------------------|--------|---|----------|----------|----------|-----|-----|---|----------|-------------|---------|
| ACEI                        | 1.05   |   | F        | -        |          | i i |     |   |          | [0.62-1.77] | 0.856   |
|                             | 0.95   |   | -        | -0       |          |     |     |   |          | [0.52-1.72] | 0.854   |
| ARB                         | 1.11   |   |          |          |          |     |     |   |          | [0.58-2.11] | 0.748   |
|                             | 1.34   |   | H        | -        | -0       |     |     |   |          | [0.66-2.71] | 0.42    |
| CCB                         | 1.42   |   | H        | -        | -        |     |     | - |          | [0.68-2.96] | 0.352   |
|                             | 2.23   |   |          | _ )—     |          |     | o   |   | <b>→</b> | [1.03-4.83] | 0.042   |
| Beta blockers               | 0.55   |   |          |          |          |     |     |   |          | [0.28-1.06] | 0.075   |
|                             | 0.83   |   | -        | 0        |          |     |     |   |          | [0.4-1.7]   | 0.608   |
| Diuretics                   | 1.03   |   | -        | -        |          | 4   |     |   |          | [0.6-1.79]  | 0.902   |
|                             | 1.06   |   | -        | <u> </u> |          | -   |     |   |          | [0.58-1.95] | 0.842   |
| Metformin                   | 0.92   |   |          | -        |          | -   |     |   |          | [0.4-2.09]  | 0.842   |
|                             | 0.96   |   |          | -0-      |          |     | -   |   |          | [0.4-2.33]  | 0.93    |
| Insulins and its analogues  | 0.78   |   | <u> </u> | -        |          | -   |     |   |          | [0.31-1.99] | 0.609   |
|                             | 0.84   |   | <b>—</b> | 0        |          |     | -   |   |          | [0.31-2.27] | 0.727   |
| Other hypoglicaemic agents  | 1.04   |   |          | -        |          |     |     |   |          | [0.43-2.52] | 0.926   |
|                             | 1.31   |   | -        | -        | <u> </u> |     |     |   | -        | [0.5-3.39]  | 0.582   |
| Statins                     | 1.03   |   |          | -        |          | 1   |     |   |          | [0.6-1.78]  | 0.921   |
|                             | 0.84   |   | -        | 0        |          |     |     |   |          | [0.46-1.54] | 0.573   |
| Other lipid-lowering agents | 1.19   |   |          | -        | -        |     |     |   | -        | [0.44-3.24] | 0.737   |
|                             | 0.51   | ł | -0-      | -        |          |     |     |   |          | [0.16-1.63] | 0.258   |
| HOSP Cohort O ICU-E         | Cohort | _ |          |          |          |     |     |   | _        |             |         |
|                             | 001011 | 0 | 0.5      | 1        | 1.5      | 2   | 2.5 | 3 | 3.5      |             |         |