An international characterisation of patients hospitalised with COVID-19 and a comparison with those previously hospitalised with influenza

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Abstract

Background
To better understand the profile of individuals with severe coronavirus disease 2019 (COVID-19), we characterised individuals hospitalised with COVID-19 and compared them to individuals previously hospitalised with influenza.

Methods
We report the characteristics (demographics, prior conditions and medication use) of patients hospitalised with COVID-19 between December 2019 and April 2020 in the US (Columbia University Irving Medical Center [CUIMC], STanford Medicine Research data Repository [STARR-OMOP], and the Department of Veterans Affairs [VA OMOP]) and Health Insurance Review & Assessment [HIRA] of South Korea. Patients hospitalised with COVID-19 were compared with patients previously hospitalised with influenza in 2014-19.

Results
6,806 (US: 1,634, South Korea: 5,172) individuals hospitalised with COVID-19 were included. Patients in the US were majority male (VA OMOP: 94%, STARR-OMOP: 57%, CUIMC: 52%), but were majority female in HIRA (56%). Age profiles varied across data sources. Prevalence of asthma ranged from 7% to 14%, diabetes from 18% to 43%, and hypertensive disorder from 22% to 70% across data sources, while between 9% and 39% were taking drugs acting on the renin-angiotensin system in the 30 days prior to their hospitalisation. Compared to 52,422 individuals hospitalised with influenza, patients admitted with COVID-19 were more likely male, younger, and, in the US, had fewer comorbidities and lower medication use.

Conclusions
Rates of comorbidities and medication use are high among individuals hospitalised with COVID-19. However, COVID-19 patients are more likely to be male and appear to be younger and, in the US, generally healthier than those typically admitted with influenza.
Introduction

The ongoing coronavirus disease 2019 (COVID-19) pandemic is placing a huge strain on health systems worldwide. While a number of studies have provided information on the clinical characteristics of individuals being hospitalised with COVID-19,[1–3] substantial uncertainty around the prevalence of comorbidities and prior medication use among this population remains. Moreover, it is not known whether those hospitalised with COVID-19 are systematically different to individuals hospitalised during previous influenza seasons. Providing such information would help to inform the current response to COVID-19.

COVID-19 shares similarities with influenza to the extent that both cause respiratory disease which can vary markedly in its severity and present with a similar constellation of symptoms, including fever, cough, myalgia, malaise and fatigue, and dyspnea. Early reports do, however, indicate that the proportion of severe infections and mortality rate are higher for COVID-19.[4] Older age and a range of underlying health conditions, such as immune deficiency, cardiovascular disease, chronic lung disease, neuromuscular disease, neurological disease, chronic renal disease, and metabolic diseases, have been associated with an increased risk of severe influenza and associated mortality.[5] While age appears to be a clear risk factor for severe COVID-19,[4] other associations are not yet well understood. Comparisons with COVID-19 are further complicated by the heterogeneity in influenza itself, with different strains resulting in different clinical presentations and associated risks. Those hospitalised with the A(H1N1)pdm09 subtype of the influenza A virus during the associated influenza pandemic in 2009 were, for example, generally younger and with fewer comorbidities than those from preceding influenza seasons.[6]

Routinely-collected health care data can improve our understanding of the characteristics of individuals hospitalised with COVID-19, with years of prior clinical observations recorded. In this study, our first aim was to characterise the demographics and medical histories of individuals hospitalised with COVID-19 across multiple institutions in two countries. Subsequently, we aimed to compare the characteristics of those hospitalised with COVID-19 with those of individuals hospitalised with influenza in previous years.

Methods

Study design

This is a cohort study based on routinely-collected electronic health records (EHRs) and claims data from the US and South Korea. The data sources used were mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).[7] The open-science Observational Health Data Sciences and Informatics (OHDSI) network maintains the OMOP CDM, and its members have developed a wide range of tools to facilitate analyses of such mapped data.[8] Two particular benefits of this approach were that contributing centres did not need to share patient-level data and common analytical code could be applied across databases.

Data sources

Data from the US and South Korea underpinned the study. EHR data from the US came from the Columbia University Irving Medical Center (CUIMC), covering NewYork-Presbyterian Hospital/Columbia University Irving Medical Center, STAnford medicine Research data Repository (STARR-OMOP), including data from Stanford Health Care,[9] and United States Department of Veterans Affairs (VA OMOP), which includes 170 medical centers. Meanwhile data from South Korea came from Health Insurance Review & Assessment (HIRA), a repository of national claims data which is collected in the process of reimbursing healthcare providers.[10] In addition, the feasibility of performing the analysis was considered for Tufts-Clinical Academic Research Enterprise Trust (CLARET), US, and the Daegu Catholic University Medical Center, a teaching hospital in Daegu, South
Korea, covered by Federated E-health Big Data for Evidence Renovation Network (FEEDER-NET). These were not included, however, due to low numbers (less than 30 individuals with COVID-19 meeting the inclusion criteria).

**Study participants**

Patients hospitalised between December 2019 and April 2020 with COVID-19 were identified on the basis of having a hospitalisation along with a confirmatory diagnosis or test result of COVID-19 within a time window from 21 days prior to admission up to the end of their hospitalisation. This time window was chosen so as to include those who had the diagnosis made prior to their hospitalisation and allow for a delay in test results or diagnoses to be made or recorded. Patients were also required to be aged 18 years or older at the time of hospitalisation. Analogous criteria were used for identifying individuals hospitalised with influenza between September 2014 to April 2019, and between September 2009 and April 2010. The motivation for this latter group was that the 2009-2010 flu epidemic included many cases of A(H1N1)pdm09 infection, which had different clinical characteristics and associated severity compared to the seasonal flu. Individuals first hospitalisation with COVID-19 or a particular flu season was considered.

For the primary analysis, individuals were required to have a minimum of 365 days of prior observation time available, so as to allow for a comprehensive capture of baseline diagnoses and medications prior to their hospitalisation. As this restriction could exclude persons with little prior health care utilisation or without sustained health insurance, we also characterised cohorts without this requirement in a sensitivity analysis.

**Characteristics at time of hospital admission**

Age at hospitalisation and sex distributions were summarised. Medication use was calculated over three time periods: 1) from a year prior up to, and including, the day of hospitalisation, 2) from 30 days prior up to, and including, the day of hospitalisation, and 3) the day of hospitalisation. Drug eras were calculated to give the span of time when an individual is assumed to be exposed to a particular active ingredient. These begin on the start date of the first drug exposure and end on the observed end date if available, or were inferred (for example, based on the number of days of supply). A persistence window of up to 30 days was permitted between two medication records for them to be considered as part of the same drug era. Individual medications were categorised using Anatomical Therapeutic Chemical (ATC) groupings. All drugs are reported in full in a dedicated interactive website (see Results section), but specific classes are reported here based on recent interest due to their potential effects (positive or negative) on COVID-19 susceptibility or severity: agents acting on the renin-angiotensin system (including angiotensin converting enzyme inhibitors (ACE) inhibitors and angiotensin II receptor blockers (ARBs)), antiepileptics, antivirals, beta blocking agents, calcium channel blockers, diuretics, drugs for acid related disorders, immunosuppressants, insulins and analogues, and lipid modifying agents (such as statins). Prevalence of medication use for each time window was determined by the proportion of persons who had at least one day during the time window overlapping with a drug era for each medication or drug class of interest. Conditions were identified on the basis of SNOMED codes, with all descendent codes included. Similarly, all recorded diagnoses are available for consultation in the accompanying website, but a list of key conditions is reported here based on recent reports of associations with COVID-19 infection or outcomes.

Age distributions in each cohort are plotted using histograms. The proportion of a cohort having a particular characteristic was described, with standardised mean differences (SMD) calculated when comparing characteristics of study cohorts. The prevalence of particular conditions or medications among those hospitalised with COVID-19 (Y axis) were compared to those hospitalised with influenza (X axis) in scatter plots, with dots on the top-left indicating a higher prevalence among those hospitalised with COVID-19 and dots on the bottom-right indicating a higher prevalence among those hospitalised with influenza.
Results

We have made all the results from this study available at an interactive website (http://evidence.ohdsi.org/Covid19CharacterizationHospitalization/). This website contains both the summary results presented here, and further details of specific medications and comorbidities for the cohorts of interest.

Patients hospitalised with COVID-19

A total of 6,806 individuals hospitalised with COVID-19 (CUIMC: 916; STARR-OMOP: 141; VA OMOP: 577; HIRA: 5,172) were included. Cohorts from CUIMC, STARR-OMOP and VA OMOP were majority male (52%, 58%, and 94% respectively), but majority female for HIRA (56%). The age distributions of those hospitalised for COVID-19 are summarised in Figure 1 (alongside those hospitalised with influenza, see below). Different patterns are seen in the various contributing databases, with predominantly younger patients in South Korea (HIRA) and most admissions in patients in their 70s in VA OMOP, with a more evenly distributed age representation in STARR-OMOP and CUIMC.

The mean (standard deviation) Charlson comorbidity index of those hospitalised with COVID-19 in the US ranged from 2.4 (3.7) for STARR-OMOP to 5.4 (3.8) for VA OMOP, and was 2.7 (2.9) in HIRA. In the US, the proportion of those hospitalised with COVID-19 who had asthma ranged from 7% to 14%, from 20% to 43% for diabetes, from 10% to 22% for heart failure, from 21% to 48% for heart disease, and from 8% to 18% for cancer. In HIRA, 14% of those hospitalised had a history of asthma, 18% had diabetes, 7% heart failure, 15% heart disease, and 8% cancer. The prevalence of hypertension ranged from 32% to 70% in the US, and was 22% in HIRA (Table 1).

For medications, the proportion of those hospitalised with COVID-19 in the US who had been taking agents acting on the renin-angiotensin system over the 30 days prior to their hospitalisation ranged from 9% to 39%, while the proportions taking immunosuppressants ranged from 3% to 10%, and from 14% to 51% for lipid modifying agents over the same time period. In South Korea, 10% had been taking agents acting on the renin-angiotensin system, 1% immunosuppressants, and 12% lipid modifying agents (Table 2). Looking at drugs of particular interest, the prevalence of use of hydroxychloroquine on the day of admission ranged from <2% to 4% in the US and was 7% in South Korea, for ACE inhibitors it ranged from 4% to 16% in the US and was 0.4% in South Korea, while for ibuprofen it ranged from 2% to 10% in the US and was 5.2% in HIRA (see http://evidence.ohdsi.org/Covid19CharacterizationHospitalization/ for full details).

Removing the requirement of having a year prior history resulted in 381 more individuals being included (CUIMC: 1,234, STARR-OMOP: 181, VA OMOP: 600, HIRA: 5,172). The inclusion of these individuals did not materially change the results (see http://evidence.ohdsi.org/Covid19CharacterizationHospitalization/ for full details).

A comparison of patients hospitalised with COVID-19 and patients hospitalised with influenza

A total of 52,422 patients hospitalised with influenza between 2014 to 2019 (CUIMC: 2,030, STARR-OMOP: 2,650, VA OMOP: 26,547, HIRA: 21,015), and 2,133 hospitalised with influenza between 2009 to 2010 were included (CUIMC:168, STARR-OMOP: 276, VA OMOP: 1,689, HIRA: 2,354). Patient characteristics of those hospitalised with COVID-19 are compared to those of individuals hospitalised with influenza between 2014 and 2019 in Figures 1 and 2, and with those hospitalised with influenza between 2009 and 2010 in Appendix Figures 1 and 2.
For CUIMC, STARR-OMOP, and HIRA, a greater proportion of those hospitalised with COVID-19 were male compared to those previously hospitalised for influenza. Of those hospitalised between 2014 to 2019 with influenza 57%, 59%, and 66% were female for CUIMC, STARR-OMOP, and HIRA, while 61%, 62% and 60% of those hospitalised between 2009 to 2010 were female in these data sources. The ages of those hospitalised with COVID-19 were generally younger compared to those hospitalised with influenza between 2014 to 2019, but those hospitalised with influenza between 2009 to 2010 were typically younger compared to both COVID-19 and to influenza 2014-2019 admissions (see Figure 1, Appendix Figure 1, and Appendix Table 2).

Overall, those hospitalised with COVID-19 had a lower prevalence of comorbidities and of use of medicines compared to those hospitalised with influenza 2014-2019 in the US data sources, but higher in the data from South Korea (Figure 2, Appendix Table 1 and Appendix Table 2).

Discussion

Summary of key findings

Patients hospitalised with COVID-19 in the US were majority male with age distributions varying across data sources, while those in South Korea were majority female and appreciably younger than typically seen in the US. Many comorbidities are common among individuals hospitalised with COVID-19 with, as an example, 32% to 70% of those hospitalised with COVID-19 in the US and 22% of those in South Korea having hypertension. Similarly, prior medication use is common with, for example, 9% to 39% in the US and 9% in South Korea taking drugs acting on the renin-angiotensin system (ACE inhibitors and ARBs) in the 30 days prior to their hospitalisation.

Comparisons with previous cohorts of patients admitted to hospital for seasonal influenza in recent years suggest that COVID-19-related admissions are seen more often in younger patients and with a higher proportion of men. In the US, those hospitalised with COVID-19 were generally healthier than patients hospitalised with influenza, but in South Korea those hospitalised with COVID-19 had more comorbidities than those hospitalised with influenza. Those hospitalised with influenza in 2009-2010, during the pandemic associated with H1N1, were younger than those hospitalised with influenza in more recent years and also overall younger than those hospitalised with COVID-19.

Findings in context

A number of studies have previously provided information on individuals hospitalised with COVID-19. While cohorts have generally been majority male, the prevalence of comorbidities have varied. In a study of 1,099 individuals who tested positive for COVID-19 in China, of whom 94% were hospitalised, 58% were male, with 7% having diabetes, 15% hypertension, and 1% cancer.[11] In a study of 191 patients with COVID-19 in two hospitals in Wuhan, China, 62% were male, 19% had diabetes, 30% had hypertension, and 1% had cancer.[12] In a study which identified 1,999 individuals who tested positive for COVID-19 and were hospitalised in New York, 63% were male, 25% had diabetes, 10% COPD, and 45% a cardiovascular condition.[13] Meanwhile, in a study of 1,482 patients admitted to hospital with COVID-19 in March 2020 in the US, 55% of these patients were male, with 28% having diabetes, 11% having COPD, and 28% having cardiovascular disease.[14] Our findings add to this emerging body of evidence. The results from our study also provide an illustration of the variation in patient characteristics across contexts, with heterogeneity seen both across the cohorts from the US and between the US and South Korea.

The comparison with influenza made in our study adds important context when considering the characteristics of those hospitalised with COVID-19. Individuals hospitalised with COVID-19 appear
to be younger and, in the US, to have fewer comorbidities than those hospitalised with influenza in previous years. Those hospitalised with COVID-19 were consistently seen to be more likely to be male.

This study has also added important information on medication use by individuals hospitalised with COVID-19, based on electronic health records and claims data. There is tremendous interest in the risks and benefits of medications such as hydroxychloroquine, ACE-inhibitors and ARBs for COVID-19, and whether other medications, such as ibuprofen, should be avoided. However, to date, there has been little evidence as to what proportion of those hospitalised with COVID-19 have previously been taking such medications. Our findings shed light on this area, and highlight the importance of further research on the benefits and harms associated with continued use of such treatments, especially those that are commonly taken amongst COVID-19 infectees with, for example, between 1 in 10 and 2 in 5 of those hospitalised with COVID-19 taking medicines acting on the renin-angiotensin system in the month before their hospital admission. The consequences of temporarily discontinuing such treatments on cardiovascular risks and mortality remain unknown.[15]

This study has described characteristics of individuals with COVID-19 at a particular point in time, at admission to hospital. While this is of particular interest given its intrinsic link with health care utilisation, this only provides a snapshot of the whole picture. Those testing positive for COVID-19 in the community can be expected to be younger and with fewer comorbidities than those hospitalised,[13,16] while those in intensive care can be expected to be older and in worse general health.[3,17] In addition, those being referred to or admitted to intensive care also seem more likely to be male.[3,17] Admission to hospital (and intensive care) is influenced by a range of supply-side factors, such as availability of beds and criteria for admission, and so the characteristics of those hospitalised does not necessarily only reflect the characteristics of those with severe illness. These factors, along with geographic variation in populations and transmission dynamics, likely explain some of the heterogeneity seen in those hospitalised with COVID-19.

Study limitations

In this study we have described the characteristics of individuals hospitalised with COVID-19 in the US and South Korea, comparing them to those of individuals hospitalised with influenza in previous years. Individuals’ characteristics have been based on routinely-collected data and so, as always, there are potential concerns around the quality of the data. In particular, individuals were considered as having COVID-19 at time of hospitalisation only if they had a test result or diagnosis indicating the disease, which will have led to the omission of individuals who can be suspected to have had the disease but lacking confirmation of it. Medical conditions may have been underestimated as they were based on the presence of condition codes, with the absence of such a record taken to indicate the absence of a disease. Meanwhile, medication records indicate that an individual was prescribed or dispensed a particular drug, but this does not necessarily mean that an individual took the drug as originally prescribed or dispensed. Our study could be subject to exposure misclassification with false positives if a patient had a dispensing but did not ingest the drug, but may also be subject to false negatives for non-adherent patients who continued their medication beyond the days supply due to stockpiling. Medication use estimates on the date of hospitalization is particularly sensitive to misclassification, and may conflate baseline concomitant drug history with immediate treatment upon admission. Comparisons of individuals hospitalised with COVID-19 with individuals previously hospitalised with influenza has limitations. In particular, observed differences may be explained by changes in clinical practice or data capture procedures over time, rather than by differences in the individuals themselves. This is likely a particular relevant drawback for any comparison of medication use.
Conclusion

Rates of comorbidities and medication use are high among individuals hospitalised with COVID-19. However, hospital admissions for COVID-19 are seen amongst younger and, in the US, generally healthier people compared to those typically admitted with seasonal influenza. Those being hospitalised for COVID-19 are also more likely to be male in comparison to those hospitalised with influenza. While protecting those groups known to be vulnerable to influenza is likely to be a useful starting point to minimize the number of hospital admissions needed for COVID-19, such strategies may need to be broadened so as to reflect the particular characteristics of individuals seen here to have been hospitalised with COVID-19.
References

1. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13. doi:10.1016/S0140-6736(20)30211-7

2. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA 2020;323:1061–9. doi:10.1001/jama.2020.1585

3. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region — Case Series. N Engl J Med Published Online First: 30 March 2020. doi:10.1056/NEJMoa2004500

4. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet 2020;3099:1–9. doi:10.1016/S1473-3099(20)30243-7

5. Mertz D, Kim TH, Johnstone J, et al. Populations at risk for severe or complicated influenza illness: systematic review and meta-analysis. BMJ Br Med J 2013;347:f5061. doi:10.1136/bmj.f5061

6. Reed C, Chaves SS, Perez A, et al. Complications Among Adults Hospitalized With Influenza: A Comparison of Seasonal Influenza and the 2009 H1N1 Pandemic. Clin Infect Dis 2014;59:166–74. doi:10.1093/cid/ciu285

7. Voss EA, Makadia R, Matcho A, et al. Feasibility and utility of applications of the common data model to multiple, disparate observational health databases. J Am Med Inf Assoc 2015;22:553–64. doi:10.1093/jamia/ocu023

8. Hripcsak G, Duke JD, Shah NH, et al. Observational Health Data Sciences and Informatics (OHDSI): Opportunities for Observational Researchers. Stud Health Technol Inform 2015;216:574–8. http://www.ncbi.nlm.nih.gov/pubmed/26262116%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4815923

9. Datta S, Posada J, Olson G, et al. A new paradigm for accelerating clinical data science at Stanford Medicine. arXiv 2020.

10. Kim J-A, Yoon S, Kim L-Y, et al. Towards Actualizing the Value Potential of Korea Health Insurance Review and Assessment (HIRA) Data as a Resource for Health Research: Strengths, Limitations, Applications, and Strategies for Optimal Use of HIRA Data. J Korean Med Sci 2017;32:718–28. https://doi.org/10.3346/jkms.2017.32.5.718

11. Guan W, Ni Z, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med Published Online First: 28 February 2020. doi:10.1056/NEJMoa2002032

12. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62. doi:10.1016/S0140-6736(20)30566-3

13. Petrillli CM, Jones SA, Yang J, et al. Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City. medRxiv 2020;2020.04.08.20057794. doi:10.1101/2020.04.08.20057794

14. Garg S, Kim L, Whitaker M, et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1–30, 2020. MMWR Morb Mortal Wkly Rep Published Online First: 2020.
15 Whiting P, Morden A, Tomlinson LA, et al. What are the risks and benefits of temporarily discontinuing medications to prevent acute kidney injury? A systematic review and meta-analysis. *BMJ Open* 2017;7:e012674. doi:10.1136/bmjopen-2016-012674

16 CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69. doi:http://dx.doi.org/10.15585/mmwr.mm6913e2external icon

17 Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* Published Online First: 6 April 2020. doi:10.1001/jama.2020.5394
Table 1: Conditions recorded over year prior for individuals hospitalised with COVID-19

| Condition                          | CUIMC (n: 916) | STARR-OMOP (n: 141) | VA OMOP (n: 577) | HIRA (n: 5,172) |
|------------------------------------|----------------|---------------------|------------------|-----------------|
| Charlson index                     | 3.6            | 2.4                 | 5.4              | 2.7             |
| Anemia                             | 14.0%          | 25.5%               | 30.0%            | 14.6%           |
| Asthma                             | 7.1%           | 13.5%               | 9.9%             | 13.6%           |
| Atrial fibrillation                | 7.8%           | <7.1%               | 15.8%            | 1.4%            |
| Chronic liver disease              | 2.5%           | <7.1%               | 6.8%             | 4.8%            |
| COPD                               | 5.3%           | <7.1%               | 28.6%            | 2.6%            |
| Dementia                           | 7.5%           | <7.1%               | 7.8%             | 3.6%            |
| Diabetes mellitus                  | 22.4%          | 19.9%               | 43.3%            | 17.9%           |
| GERD                               | 9.1%           | 18.4%               | 26.9%            | 29.1%           |
| Heart disease                      | 25.4%          | 21.3%               | 48.2%            | 15.3%           |
| Heart failure                      | 10.2%          | 10.6%               | 22.2%            | 7.2%            |
| Hyperlipidemia                     | 23.3%          | 32.6%               | 55.8%            | 30.6%           |
| Hypertensive disorder              | 33.8%          | 31.9%               | 69.7%            | 21.8%           |
| Ischemic heart disease             | 7.3%           | <7.1%               | 15.6%            | 7.2%            |
| Malignant neoplasm of respiratory system | 1.4%          | <7.1%               | 3.1%             | 1.5%            |
| Cancer                             | 7.8%           | 14.9%               | 18.4%            | 8.3%            |
| Peripheral vascular disease        | 4.7%           | <7.1%               | 10.6%            | 7.4%            |
| Renal impairment                   | 18.7%          | 17.0%               | 32.9%            | 5.4%            |
| Venous thrombosis                  | 2.5%           | <7.1%               | 4.0%             | 0.9%            |
| Viral hepatitis                    | 2.3%           | <7.1%               | 5.9%             | 5.6%            |

CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment. COPD: Chronic obstructive pulmonary disease; GERD: Gastroesophageal reflux disease. Exact proportions have not been reported where counts were less than 10.
Table 2: Prior medications of individuals hospitalised with COVID-19

|                                | CUIMC (n: 916) | STARR-OMOP (n: 141) | VA OMOP (n: 577) | HIRA (n: 4,123) |
|--------------------------------|---------------|----------------------|------------------|----------------|
| **Antineoplastic and immunomodulating agents** |               |                      |                  |                |
| Year prior to hospitalisation  | 8.7%          | 21.3%                | 13.2%            | 4.6%           |
| 30 days prior to hospitalisation | 5.0%      | 16.3%                | 7.1%             | 2.1%           |
| At hospitalisation             | 3.2%          | 14.9%                | 4.9%             | 1.4%           |
| **Agents acting on the renin-angiotensin system** |               |                      |                  |                |
| Year prior to hospitalisation  | 24.7%         | 14.2%                | 49.6%            | 12.2%          |
| 30 days prior to hospitalisation | 14.6%    | 8.5%                 | 38.5%            | 9.8%           |
| At hospitalisation             | 11.9%         | 7.8%                 | 33.1%            | 8.7%           |
| **Antiepileptics**             |               |                      |                  |                |
| Year prior to hospitalisation  | 15.8%         | 19.1%                | 33.4%            | 11.8%          |
| 30 days prior to hospitalisation | 6.3%     | 14.9%                | 22.7%            | 3.8%           |
| At hospitalisation             | 5.0%          | 10.6%                | 16.6%            | 1.4%           |
| **Anti-inflammatory and antirheumatic products** |               |                      |                  |                |
| Year prior to hospitalisation  | 23.9%         | 27.7%                | 46.1%            | 59.7%          |
| 30 days prior to hospitalisation | 9.1%    | 17.0%                | 16.8%            | 21.3%          |
| At hospitalisation             | 5.6%          | 14.2%                | 9.9%             | 10.3%          |
| **Antithrombotic agents**      |               |                      |                  |                |
| Year prior to hospitalisation  | 36.5%         | 31.9%                | 55.8%            | 36.4%          |
| 30 days prior to hospitalisation | 20.6%   | 28.4%                | 42.1%            | 15.2%          |
| At hospitalisation             | 17.8%         | 27.0%                | 35.5%            | 9.6%           |
| Drugs                        | Year prior to hospitalisation | 30 days prior to hospitalisation | At hospitalisation |
|-----------------------------|------------------------------|----------------------------------|-------------------|
| **Antivirals**              |                              |                                  |                   |
|                             | 8.4%                         | 21.3%                            | 12.5%             | 21.6%             |
|                             | 3.1%                         | 17.7%                            | 7.1%              | 15.3%             |
|                             | 2.2%                         | 15.6%                            | 5.2%              | 14.4%             |
| **Beta blocking agents**    |                              |                                  |                   |
|                             | 23.4%                        | 17.7%                            | 44.4%             | 6.9%              |
|                             | 12.1%                        | 11.3%                            | 36.0%             | 3.8%              |
|                             | 9.3%                         | 11.3%                            | 31.0%             | 3.0%              |
| **Calcium channel blockers**|                              |                                  |                   |
|                             | 21.3%                        | 14.2%                            | 35.0%             | 10.7%             |
|                             | 11.8%                        | 8.5%                             | 27.0%             | 8.6%              |
|                             | 9.8%                         | 7.8%                             | 24.3%             | 7.5%              |
| **Diuretics**               |                              |                                  |                   |
|                             | 23.8%                        | 19.9%                            | 42.6%             | 7.2%              |
|                             | 13.8%                        | 17.0%                            | 33.1%             | 5.0%              |
|                             | 11.2%                        | 17.0%                            | 28.4%             | 4.4%              |
| **Drugs for acid related disorders** |                        |                                  |                   |
|                             | 32.9%                        | 36.2%                            | 52.0%             | 63.1%             |
|                             | 16.6%                        | 28.4%                            | 36.2%             | 21.9%             |
|                             | 13.1%                        | 26.2%                            | 28.9%             | 14.2%             |
| **Immunosuppressants**      |                              |                                  |                   |
|                             | 5.3%                         | 13.5%                            | 5.7%              | 2.2%              |
|                             | 3.3%                         | 9.9%                             | 3.5%              | 0.8%              |
|                             | 2.7%                         | 9.9%                             | 2.6%              | 0.5%              |
|                      | In 17.2% | In 15.6% | In 22.9% | In 1.2% |
|----------------------|----------|----------|----------|---------|
| Year prior to hospitalisation | 17.2%    | 15.6%    | 22.9%    | 1.2%    |
| 30 days prior to hospitalisation | 11.1%    | 12.8%    | 18.4%    | 0.8%    |
| At hospitalisation   | 9.8%     | 12.8%    | 14.6%    | 0.5%    |

|                      | In 27.8% | In 18.4% | In 61.9% | In 15.5% |
|----------------------|----------|----------|----------|----------|
| Year prior to hospitalisation | 27.8%    | 18.4%    | 61.9%    | 15.5%    |
| 30 days prior to hospitalisation | 14.7%    | 13.5%    | 50.8%    | 12.3%    |
| At hospitalisation   | 10.4%    | 12.8%    | 43.8%    | 10.7%    |

CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment.
Figure 1: Age of patients hospitalised with COVID-19 compared to patients hospitalised with influenza

Individuals hospitalised with COVID-19 between December 2019 and April 2020 compared with those hospitalised with influenza between September 2014 to April 2019. Proportion of cohorts by 5-year age groups, with groups with counts of less than 10 omitted. CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment.
Figure 2: Characteristics of COVID-19 patients compared to 2014-2019 Influenza patients

The plot compares demographics (age and sex), conditions (recorded over the year prior and up to day of hospitalisation), and medications (1) from a year prior to day of hospitalisation, 2) from 30 days prior to day of hospitalisation, and 3) on day of hospitalisation). Each dot represents one of these covariates with the colour indicating the absolute value of the standardised mean difference (SMD), with a SMD above 0.1 taken to indicate a difference in the prevalence of a particular covariate. The proportion male, with heart disease, and taking immunosuppressants (over the 30 days prior to hospitalisation) are shown for illustration. CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment.
Ethical approvals

All the data partners received Institutional Review Board (IRB) approval or exemption. STARR-OMOP had approval from IRB Panel #8 (RB-53248) registered to Leland Stanford Junior University under the Stanford Human Research Protection Program (HRPP). The use of VA data was reviewed by the Department of Veterans Affairs Central Institutional Review Board (IRB) and was determined to meet the criteria for exemption under Exemption Category 4(3) and approved the request for Waiver of HIPAA Authorization. The research was approved by the Columbia University Institutional Review Board as an OHDSI network study. The IRB number for use of HIRA data was AJIB-MED-EXP-20-065.

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Appendix figure 1. Age of patients hospitalised with COVID-19 compared to patients hospitalised with influenza

Individuals hospitalised with COVID-19 between December 2019 and April 2020 compared with those hospitalised with influenza between September 2009 to April 2010. Proportion of cohorts by 5-year age groups, with counts of less than 10 omitted. CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment.
Appendix figure 2. Characteristics of COVID-19 patients compared to 2009-2010 Influenza patients

The plot compares demographics (age and sex), conditions (recorded over the year prior and up to day of hospitalisation), and medications (1) from a year prior to day of hospitalisation, 2) from 30 days prior to day of hospitalisation, and 3) on day of hospitalisation). Each dot represents one of these covariates with the colour indicating the absolute value of the standardised mean difference (SMD), with a SMD above 0.1 taken to indicate a difference in the prevalence of a particular covariate. The proportion male, with heart disease, and taking immunosuppressants (over the 30 days prior to hospitalisation) are shown for illustration. CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment.
Appendix table 1. Characteristics of individuals hospitalised with COVID-19 compared with those hospitalised with influenza in 2015-2019

| Demographics | CUIMC COVID-19 | CUIMC Influenza 2014-19 | CUIMC StdDif | STARR-OMOP COVID-19 | STARR-OMOP Influenza 2014-19 | STARR-OMOP StdDif | VA OMOP COVID-19 | VA OMOP Influenza 2014-19 | VA OMOP StdDif | HIRA COVID-19 | HIRA Influenza 2014-19 | HIRA StdDif |
|--------------|----------------|-------------------------|--------------|---------------------|--------------------------|----------------------|-----------------|---------------------------|----------------|----------------|------------------------|-------------|
| Sex: male    | 51.7%          | 43.3%                   | 0.09         | 57.4%               | 41.4%                    | 0.16                 | 94.3%           | 94.1%                     | 0.00           | 44.3%          | 34.5%                  | 0.11        |
| Sex: female  | 48.3%          | 56.7%                   | -0.08        | 42.6%               | 58.6%                    | -0.16                | 5.7%            | 5.9%                      | -0.01         | 55.7%          | 65.5%                  | -0.09       |
| Age group: 15-19 | <1.1%        | 1.1%                    | <7.1%        | 2.6%                | <7.1%                    | 6.1%                | <1.1%           | 0.4%                      | 13.1%         | 5.8%           | 0.17                   |            |
| Age group: 20-24 | 1.2%         | 3.0%                    | -0.09        | <7.1%               | 6.1%                     | <1.1%               | <1.1%           | 0.4%                      | 13.1%         | 5.8%           | 0.17                   |            |
| Age group: 25-29 | 3.6%         | 3.9%                    | -0.01        | <7.1%               | 6.8%                     | <1.1%               | 0.4%            | 13.1%                     | 5.8%          | 0.17            |                        |            |
| Age group: 30-34 | 5.6%         | 3.6%                    | 0.07         | 7.8%                | 6.6%                     | 0.03                | <1.1%           | 0.8%                      | 9.1%          | 8.0%           | 0.03                   |            |
| Age group: 35-39 | 5.7%         | 3.2%                    | 0.08         | <7.1%               | 7.9%                     | 0.24                | 1.0%            | 0.08                      | 9.7%          | 9.6%           | 0.00                   |            |
| Age group: 40-44 | 5.1%         | 3.0%                    | 0.07         | 13.5%               | 6.7%                     | 0.15                | 2.6%            | 1.1%                      | 0.08          | 8.4%           | 7.9%                   | 0.01        |
| Age group: 45-49 | 4.1%         | 3.7%                    | 0.01         | <7.1%               | 7.9%                     | 0.15                | 2.6%            | 1.1%                      | 0.08          | 8.4%           | 7.9%                   | 0.01        |
| Age group: 50-54 | 8.5%         | 5.9%                    | 0.07         | <7.1%               | 6.7%                     | 0.10                | 9.2%            | 7.5%                      | 0.04          | 7.2%           | 10.2%                  | -0.07       |
| Age group: 55-59 | 9.3%         | 6.6%                    | 0.07         | 12.1%               | 7.7%                     | 0.10                | 13.9%           | 12.4%                     | 0.03          | 6.5%           | 7.7%                   | -0.03       |
| Age group: 60-64 | 9.5%         | 8.5%                    | 0.02         | 7.8%                | 8.3%                     | -0.01               | 13.9%           | 12.4%                     | 0.03          | 6.5%           | 7.7%                   | -0.03       |
| Age group: 65-69 | 10.3%        | 10.0%                   | 0.01         | 7.8%                | 8.3%                     | -0.01               | 12.8%           | 19.1%                     | -0.11         | 4.5%           | 5.6%                   | -0.03       |
| Age group: 70-74 | 9.8%         | 9.4%                    | 0.01         | <7.1%               | 7.8%                     | 0.15                | 19.8%           | 19.7%                     | 0.00          | 3.6%           | 5.1%                   | -0.05       |
| Age group: 75-79 | 8.8%         | 10.2%                   | -0.03        | 8.5%                | 5.7%                     | 0.07                | 11.1%           | 9.6%                      | 0.03          | 3.6%           | 5.3%                   | -0.06       |
| Age group: 80-84 | 6.8%         | 9.9%                    | -0.08        | <7.1%               | 4.8%                     | 0.07                | 5.0%            | 8.2%                      | -0.09         | 2.3%           | 4.2%                   | -0.07       |
| Age group: 85-89 | 4.9%         | 8.4%                    | -0.10        | <7.1%               | 5.3%                     | 0.07                | 5.9%            | 7.3%                      | -0.04         | 1.2%           | 2.3%                   | -0.06       |
| Age group: 90-94 | 5.0%         | 6.6%                    | -0.05        | 0.7%                |                          |                    | 3.1%            | 5.3%                      | -0.08         | 0.4%           | 0.8%                   | -0.04       |
| Age group: 95-99 | <1.1%        | 2.4%                    |              |                   |                          |                    | <1.7%           | 1.6%                      |              | <0.1%         | 0.1%                   |            |
| Age group: 100-04 | <1.1%        | 0.6%                    |              |                   |                          |                    | 0.1%            |                          |              |                |                        |            |

**Conditions**

| Condition               | CUIMC 2014-19 | CUIMC 2014-19 | CUIMC StdDif | STARR-OMOP 2014-19 | STARR-OMOP 2014-19 | STARR-OMOP StdDif | VA OMOP 2014-19 | VA OMOP 2014-19 | VA OMOP StdDif | HIRA 2014-19 | HIRA 2014-19 |
|-------------------------|---------------|---------------|--------------|-------------------|-------------------|-------------------|-----------------|-----------------|----------------|---------------|---------------|
| Charlson index          | 3.6           | 5.8           | -0.38        | 2.4               | 2.9               | -0.10             | 5.4             | 5.9             | -0.09          | 2.7           | 0.5           | 0.72          |
| Anemia                  | 14.0%         | 26.1%         | -0.19        | 25.5%             | 23.2%             | 0.03              | 30.0%           | 27.3%           | 0.04           | 14.6%         | 4.4%          | 0.23          |
| Asthma                  | 7.1%          | 21.7%         | -0.27        | 13.5%             | 17.5%             | -0.07             | 9.9%            | 8.3%            | 0.04           | 13.6%         | 10.2%         | 0.07          |
| Atrial fibrillation     | 7.8%          | 20.3%         | -0.24        | <7.1%             | 10.7%             | 0.15              | 15.8%           | 20.8%           | -0.08          | 1.4%          | 0.8%          | 0.04          |
| Chronic liver disease   | 2.5%          | 5.0%          | -0.09        | <7.1%             | 5.2%              | 0.07              | 6.8%            | 7.5%            | -0.02          | 4.8%          | 1.5%          | 0.13          |
| COPD                    | 5.3%          | 18.7%         | -0.27        | <7.1%             | 8.0%              | 0.07              | 28.6%           | 43.0%           | -0.17          | 2.6%          | 1.7%          | 0.04          |
| Condition                                      | Year Prior to Index Date | 30 Days Prior to Index Date | On Index Date |
|-----------------------------------------------|--------------------------|-----------------------------|---------------|
| **Dementia**                                  | 7.5% 9.5% -0.05 <7.1%    | 3.4%                        | 7.8% 10.2% -0.06 | 3.6% 1.1% 0.12 |
| **Diabetes mellitus**                         | 22.4% 32.6% -0.14 19.9%  | 20.9% -0.02 43.3% 43.1%  | 0.00 17.9% 15.0% 0.05 |
| **GERD**                                      | 9.1% 16.7% -0.15 18.4%  | 19.1% -0.01 26.9% 29.1%  | -0.03 29.1% 8.8% 0.33 |
| **Heart disease**                             | 25.4% 53.5% -0.32 21.3%  | 32.5% -0.15 48.2% 58.2%  | -0.10 15.3% 5.1% 0.23 |
| **Heart failure**                             | 10.2% 26.0% -0.26 10.6%  | 11.5% -0.02 22.2% 25.7%  | -0.05 7.2% 1.6% 0.19 |
| **Hyperlipidemia**                            | 23.3% 33.8% -0.14 32.6%  | 31.8% 0.01 55.8% 58.5%  | -0.03 30.6% 16.4% 0.21 |
| **Hypertensive disorder**                     | 33.8% 51.4% -0.19 31.9%  | 37.9% -0.07 69.7% 71.8%  | -0.02 21.8% 7.2% 0.27 |
| **Ischemic heart disease**                    | 7.3% 15.5% -0.17 <7.1%   | 7.8% 15.6% 21.3% -0.09 7.2% 2.0% 0.17 |
| **Cancer**                                    | 7.8% 16.7% -0.18 14.9%   | 20.0% -0.09 18.4% 21.4% -0.05 8.3% 0.7% 0.25 |
| **Peripheral vascular disease**               | 4.7% 5.9% -0.04 <7.1%   | 3.1% 10.6% 12.7% -0.04 7.4% 0.8% 0.23 |
| **Renal impairment**                          | 18.7% 35.5% -0.23 17.0%  | 21.4% -0.07 32.9% 32.2% 0.01 5.4% 0.7% 0.19 |
| **Venous thrombosis**                         | 2.5% 7.4% -0.16 <7.1%   | 4.2% 4.0% 4.0% 0.00 0.9% |
| **Viral hepatitis**                           | 2.3% 3.7% -0.06 <7.1%   | 3.9% 5.9% 6.3% -0.01 5.6% 2.0% 0.13 |
| **Medications**                               |                          |                             |               |
| **Antineoplastic and immunomodulating agents**| 8.7% 21.1% -0.23 21.3%  | 22.8% -0.02 13.2% 13.5%  | -0.01 4.6% 0.3% 0.20 |
| **Antineoplastic and immunomodulating agents**| 5.0% 16.6% -0.25 16.3%  | 18.8% -0.04 7.1% 8.5%  | -0.04 2.1% 0.3% 0.12 |
| **Antineoplastic and immunomodulating agents**| 3.2% 14.5% -0.27 14.9%  | 17.6% -0.05 4.9% 6.7%  | -0.05 1.4% 0.3% 0.09 |
| **Agents acting on the renin-angiotensin system**| 24.7% 36.7% -0.15 14.2%  | 20.6% -0.11 49.6% 50.8%  | -0.01 12.2% 2.9% 0.24 |
| **Agents acting on the renin-angiotensin system**| 14.6% 24.9% -0.16 8.5%  | 16.6% -0.16 38.5% 41.0%  | -0.03 9.8% 2.9% 0.19 |
| **Agents acting on the renin-angiotensin system**| 11.9% 23.5% -0.19 7.8%  | 16.0% -0.17 33.1% 38.8%  | -0.07 8.7% 2.9% 0.17 |
| Drug Category                                              | Year Prior to Index Date | 30 Days Prior to Index Date | On Index Date      |
|------------------------------------------------------------|--------------------------|----------------------------|--------------------|
| Antiepileptics                                            | 15.8%                    | 6.3%                       | 5.0%               |
| Anti-inflammatory and antirheumatic products               | 23.9%                    | 9.1%                       | 5.6%               |
| Antithrombotic agents                                     | 36.5%                    | 20.6%                      | 17.8%              |
| Antivirals                                                | 8.4%                     | 3.1%                       | 2.2%               |
| Beta blocking agents                                      | 23.4%                    | 12.1%                      | 1.7%               |

| Drug Category                                              | Year Prior to Index Date | 30 Days Prior to Index Date | On Index Date      |
|------------------------------------------------------------|--------------------------|----------------------------|--------------------|
| Antiepileptics                                            | 24.8%                    | 16.5%                      | 15.3%              |
| Anti-inflammatory and antirheumatic products               | 34.4%                    | 20.0%                      | 17.2%              |
| Antithrombotic agents                                     | 75.6%                    | 65.1%                      | 17.6%              |
| Antivirals                                                | 49.4%                    | 45.0%                      | 43.2%              |
| Beta blocking agents                                      | 40.0%                    | 31.1%                      | 31.1%              |
| Drug Class                                | Year Prior to Index Date | 30 Days Prior to Index Date | On Index Date          |
|------------------------------------------|--------------------------|-----------------------------|------------------------|
| **Beta blocking agents**:                |                          |                             |                        |
| (on index date)                          | 9.3% 30.1%               | -0.33 11.3%                 | -0.12 31.0%            | -0.16 3.0% 1.2% 0.09 |
| Calcium channel blockers (year prior to  | 21.3% 32.9%              | -0.16 14.2%                 | -0.07 35.0%            | 0.01 10.7% 3.0% 0.21 |
| index date)                              |                          | 18.2%                       | 34.4%                  |                        |
| Calcium channel blockers (30 days prior  | 11.8% 22.4%              | -0.18 8.5%                  | -0.12 27.0%            | 0.00 8.6% 3.0% 0.16   |
| to index date)                           |                          | 14.1%                       | 26.8%                  |                        |
| Calcium channel blockers (on index date) | 9.8% 21.1%               | -0.20 7.8%                  | -0.12 24.3%            | -0.02 7.5% 3.0% 0.14  |
| Diuretics (year prior to index date)     | 23.8% 42.6%              | -0.23 19.9%                 | -0.05 42.6%            | -0.05 7.2% 3.3% 0.12  |
| Diuretics (30 days prior to index date)  | 13.8% 32.2%              | -0.27 17.0%                 | 0.00 33.1%             | -0.05 5.0% 3.3% 0.06  |
| Diuretics (on index date)                | 11.2% 30.1%              | -0.29 17.0%                 | 0.01 28.4%             | -0.08 4.4% 3.3% 0.04  |
| Drugs for acid related disorders (year   | 32.9% 60.2%              | -0.28 36.2%                 | -0.03 52.0%            | -0.08 63.1% 45.0% 0.17|
| prior to index date)                     |                          | 38.8%                       | 60.7%                  |                        |
| Drugs for acid related disorders (30 days| 16.6% 45.0%              | -0.36 28.4%                 | -0.01 36.2%            | -0.12 21.9% 45.0% -0.28|
| prior to index date)                     |                          | 29.1%                       | 47.5%                  |                        |
| Drugs for acid related disorders (on     | 13.1% 42.5%              | -0.39 26.2%                 | -0.02 28.9%            | -0.19 14.2% 45.0% -0.40|
| index date)                              |                          | 27.8%                       | 44.8%                  |                        |
| Immunosuppressants (year prior to index  | 5.3% 13.3%               | -0.19 13.5%                 | 13.3%                  | 0.00 5.7% 5.4% 0.01   |
| date)                                    |                          | 13.5%                       |                        | 2.2% 0.1% 0.14         |
| Immunosuppressants (30 days prior to     | 3.3% 11.2%               | -0.21 9.9%                  | 11.2%                  | -0.03 3.5% 4.1% -0.02 |
| index date)                              |                          | 9.9%                        |                        | 0.8% 0.1% 0.07         |
| Immunosuppressants (on index date)       | 2.7% 10.4%               | -0.21 9.9%                  | 10.8%                  | -0.02 2.6% 3.7% -0.04  |
| Insulins and analogues (year prior to    | 17.2% 32.0%              | -0.21 15.6%                 | -0.03 22.9%            | -0.10 1.2% 2.0% -0.04  |
| index date)                              |                          | 17.6%                       | 30.0%                  |                        |
| Category                                      | 30 days prior to index date | 30 days prior to index date | Difference |
|----------------------------------------------|----------------------------|-----------------------------|------------|
| Insulins and analogues                       | 11.1%                      | 22.5%                       | -0.20      |
| Lipid modifying agents                       | 27.8%                      | 44.0%                       | -0.19      |
| Lipid modifying agents                       | 14.7%                      | 35.2%                       | -0.29      |
| Lipid modifying agents                       | 10.4%                      | 34.0%                       | -0.35      |
| Lipid modifying agents (on index date)       | 9.8%                       | 21.4%                       | -0.21      |
| Lipid modifying agents (on index date)       | 27.8%                      | 44.0%                       | -0.19      |
| Lipid modifying agents (on index date)       | 14.7%                      | 35.2%                       | -0.29      |
| Lipid modifying agents (on index date)       | 10.4%                      | 34.0%                       | -0.35      |

CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment. COPD: Chronic obstructive pulmonary disease; GERD: Gastroesophageal reflux disease. Exact proportions have not been reported where counts were less than 10.
Appendix table 2. Characteristics of individuals hospitalised with COVID-19 compared with those hospitalised with influenza in 2009-2010

| Conditions                  | CUIMC COVID-19 | CUIMC Influenza 2009-10 | CUIMC StdDif | STARR-OMOP COVID-19 | STARR-OMOP Influenza 2009-10 | STARR-OMOP StdDif | VA OMOP COVID-19 | VA OMOP Influenza 2009-10 | VA OMOP StdDif | HIRA COVID-19 2009-10 | HIRA Influenza 2009-10 | HIRA StdDif |
|-----------------------------|----------------|-------------------------|--------------|---------------------|-----------------------------|---------------------|------------------|-------------------------|----------------|--------------------------|-----------------------|-------------|
| **Demographics**            |                |                         |              |                     |                             |                     |                  |                         |                |                          |                       |             |
| Sex: male                   | 51.7%          | 39.3%                   | 0.13         | 57.4%               | 38.4%                       | 0.19                | 94.3%           | 91.4%                   | 0.02           | 44.3%                    | 40.6%                 | 0.04         |
| Sex: female                 | 48.3%          | 60.7%                   | -0.12        | 42.6%               | 61.6%                       | -0.19               | 5.7%            | 8.6%                    | -0.08          | 55.7%                    | 59.4%                 | -0.03        |
| Age group: 15-19            | <1.1%          | <6.0%                   | <7.1%        | 5.1%                |                             |                     |                  |                         |                |                          |                       |             |
| Age group: 20-24            | 1.2%           | 7.1%                    | -0.20        | <7.1%               | 17.8%                       | <1.7%               | <0.6%           | 11.5%                   | 9.7%           | 0.04                     |                       |             |
| Age group: 25-29            | 3.6%           | 8.9%                    | -0.15        | <7.1%               | 12.0%                       | <1.7%               | 2.7%            | 13.1%                   | 17.3%          | -0.08                    |                       |             |
| Age group: 30-34            | 5.6%           | <6.0%                   | 7.8%         | 8.0%                | -0.01                       | <1.7%               | 2.1%            | 9.1%                    | 11.9%          | -0.06                    |                       |             |
| Age group: 35-39            | 5.7%           | <6.0%                   | <7.1%        | 7.6%                |                             | 2.4%                | 2.4%            | 0.00                    | 9.7%           | 7.8%                     | 0.05                  |             |
| Age group: 40-44            | 5.1%           | <6.0%                   | 13.5%        | 7.2%                | 0.14                        | 2.6%                | 4.1%            | -0.06                   | 8.4%           | 7.1%                     | 0.03                  |             |
| Age group: 45-49            | 4.1%           | 8.3%                    | -0.12        | <7.1%               | 9.1%                        | 3.8%                | 7.8%            | -0.12                   | 8.2%           | 8.6%                     | -0.01                 |             |
| Age group: 50-54            | 8.5%           | 9.5%                    | -0.02        | <7.1%               | 7.2%                        | 6.4%                | 14.0%           | -0.17                   | 8.4%           | 12.4%                    | -0.09                 |             |
| Age group: 55-59            | 9.3%           | 11.3%                   | -0.04        | 12.1%               | 4.3%                        | 0.19                | 9.2%            | 17.7%                   | -0.16          | 7.2%                     | 8.7%                   | -0.04        |
| Age group: 60-64            | 9.5%           | 10.7%                   | -0.03        | 7.8%                | 5.8%                        | 0.05                | 13.9%           | 21.0%                   | -0.12          | 6.5%                     | 4.4%                   | 0.06         |
| Age group: 65-69            | 10.3%          | 6.5%                    | 0.09         | 7.8%                | 5.1%                        | 0.08                | 12.8%           | 9.6%                    | 0.07           | 4.5%                     | 3.6%                   | 0.03         |
| Age group: 70-74            | 9.8%           | 9.5%                    | 0.01         | <7.1%               | <3.6%                       | 19.8%               | 5.3%            | 0.29                    | 3.6%           | 2.9%                     | 0.03                  |             |
| Age group: 75-79            | 8.8%           | 6.5%                    | 0.06         | 8.5%                | <3.6%                       | 11.1%               | 5.0%            | 0.15                    | 3.6%           | 1.6%                     | 0.09                  |             |
| Age group: 80-84            | 6.8%           | <6.0%                   | <7.1%        | <3.6%               |                             | 5.0%                | 3.4%            | 0.06                    | 2.3%           | 1.0%                     | 0.07                  |             |
| Age group: 85-89            | 4.9%           | <6.0%                   | <7.1%        | 5.9%                | 3.4%                        | 0.08                | 1.2%            | 0.3%                    | 0.07           |                         |                       |             |
| Age group: 90-94            | 5.0%           | <6.0%                   | 3.1%         | 0.7%                | 0.12                        | 0.4%                | <0.2%           |                         |                |                          |                       |             |
| Age group: 95-99            | <1.1%          | <6.0%                   | <1.7%        | <0.6%               | <0.1%                       |                     |                |                         |                |                          |                       |             |
| Age group: 100-04           | <1.1%          | <6.0%                   |              |                     |                             |                     |                |                         |                |                          |                       |             |
| **Conditions**              |                |                         |              |                     |                             |                     |                |                         |                |                          |                       |             |
| Charlson index              | 3.6            | 4.8                     | -0.21        | 2.4                 | 1.3                         | 0.25                | 5.4             | 4.2                     | 0.24           | 2.7                      | 0.4                    | 0.73         |
| Anemia                      | 14.0%          | 23.8%                   | -0.16        | 25.5%               | 14.9%                       | 0.17                | 30.0%           | 23.0%                   | 0.10           | 14.6%                    | 3.6%                   | 0.26         |
| Asthma                      | 7.1%           | 27.4%                   | -0.34        | 13.5%               | 11.6%                       | 0.04                | 9.9%            | 12.6%                   | -0.06          | 13.6%                    | 10.3%                  | 0.07         |
| Atrial fibrillation         | 7.8%           | 10.7%                   | -0.07        | <7.1%               | 5.8%                        | 15.8%               | 9.9%            | 0.12                    | 1.4%           |                         |                       |             |
| Chronic liver disease       | 2.5%           | 7.7%                    | -0.16        | <7.1%               | <3.6%                       | 6.8%                | 7.6%            | -0.02                   | 4.8%           | 2.8%                     | 0.07                  |             |
| Condition                        | 5.3%  | 14.3% | -0.20 | <7.1% | <3.6% | 28.6% | 31.0% | -0.03 | 2.6% | 3.1% | -0.02 |
|---------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|-------|
| **COPD**                        |       |       |       |       |       |       |       |       |      |      |       |
| **Dementia**                    | 7.5%  | <6.0% | -0.09 | 19.9% | 12.0% | 0.14  | 43.3% | 36.1% | 0.08 | 17.9% | 7.0%  |
| **Diabetes mellitus**           | 22.4% | 28.6% | -0.10 | 18.4% | 12.0% | 0.12  | 26.9% | 27.2% | 0.00 | 29.1% | 2.2%  |
| **GERD**                        | 25.4% | 47.0% | -0.25 | 21.3% | 21.4% | 0.00  | 48.2% | 43.9% | 0.04 | 15.3% | 3.9%  |
| **Heart disease**               | 0.2%  | 31.0% | <7.1% |       |       |       |       |       |      |      |       |
| **Heart failure**               | 25.4% | 47.0% | -0.25 | 21.3% | 21.4% | 0.00  | 48.2% | 43.9% | 0.04 | 15.3% | 3.9%  |
| **Hyperlipidemia**              | 23.3% | 47.0% | -0.25 | 21.3% | 21.4% | 0.00  | 48.2% | 43.9% | 0.04 | 15.3% | 3.9%  |
| **Hypertensive disorder**       | 0.2%  | 31.0% | <7.1% |       |       |       |       |       |      |      |       |
| **Dementia**                    | 10.2% | 22.6% | -0.22 | 10.6% | 8.3%  | 0.05  | 22.2% | 15.7% | 0.11 | 7.2%  | 1.3%  |
| **Diabetes mellitus**           | 3.1%  | 6.5%  | -0.14 | <7.1% | <3.6% | 5.9%  | 9.5%  | -0.09 | 5.6% | 3.4% | 0.07  |
| **Medications**                 |       |       |       |       |       |       |       |       |      |      |       |
| Antineoplastic and immunomodulating agents (year prior to index date) | 8.7%  | 12.5% | -0.08 | 21.3% | 16.3% | 0.08  | 13.2% | 14.0% | -0.02 | 4.6% | 0.3%  |
| Antineoplastic and immunomodulating agents (30 days prior to index date) | 5.0%  | 10.7% | -0.14 | 16.3% | 12.7% | 0.07  | 7.1%  | 8.8%  | -0.04 | 2.1% | 0.3%  |
| Antineoplastic and immunomodulating agents (on index date) | 3.2%  | 9.5%  | -0.18 | 14.9% | 11.2% | 0.07  | 4.9%  | 7.2%  | -0.07 | 1.4% | 0.3%  |
| Agents acting on the renin-angiotensin system (year prior to index date) | 24.7% | 34.5% | -0.13 | 14.2% | 12.3% | 0.04  | 49.6% | 50.4% | -0.01 | 12.2% | 2.9%  |
| Agents acting on the renin-angiotensin system (30 days prior to index date) | 14.6% | 27.4% | -0.20 | 8.5%  | 7.6%  | 0.02  | 38.5% | 41.3% | -0.03 | 9.8% | 2.9%  |
| Agents acting on the renin-angiotensin system (on index date) | 11.9% | 26.2% | -0.23 | 7.8%  | 6.9%  | 0.02  | 33.1% | 40.1% | -0.08 | 8.7% | 2.9%  |
| Antiepileptics (year prior to index date) | 15.8% | 11.3% | 0.09  | 19.1% | 8.7%  | 0.20  | 33.4% | 32.0% | 0.02  | 7.3% | 0.9%  |
| Category (Year prior to index date) | 6.3% | 9.5% | 14.9% | 4.3% | 0.24 | 22.7% | 25.3% | -0.04 | 3.0% | 0.9% | 0.11 |
|-----------------------------------|------|------|-------|------|------|-------|-------|-------|------|------|-------|
| Antiepileptics (30 days prior to index date) | 5.0% | 9.5% | 10.6% | 4.3% | 0.16 | 16.6% | 23.8% | -0.11 | 2.2% | 0.9% | 0.07 |
| Anti-inflammatory and antirheumatic products (year prior to index date) | 23.9% | 22.0% | 0.03 | 27.7% | 21.0% | 0.10 | 46.1% | 41.6% | 0.05 | 59.7% | 40.7% | 0.19 |
| Anti-inflammatory and antirheumatic products (30 days prior to index date) | 9.1% | 13.7% | -0.10 | 17.0% | 11.6% | 0.10 | 16.8% | 20.2% | -0.06 | 21.3% | 40.7% | -0.25 |
| Anti-inflammatory and antirheumatic products (on index date) | 5.6% | 13.7% | -0.18 | 14.2% | 10.5% | 0.07 | 9.9% | 17.0% | -0.14 | 10.3% | 40.5% | -0.42 |
| Antithrombotic agents (year prior to index date) | 36.5% | 55.4% | -0.20 | 31.9% | 27.9% | 0.05 | 55.8% | 63.5% | -0.07 | 36.4% | 13.2% | 0.33 |
| Antithrombotic agents (30 days prior to index date) | 20.6% | 44.0% | -0.29 | 28.4% | 18.1% | 0.15 | 42.1% | 51.8% | -0.10 | 15.2% | 13.2% | 0.04 |
| Antithrombotic agents (on index date) | 17.8% | 42.3% | -0.32 | 27.0% | 17.0% | 0.15 | 35.5% | 49.7% | -0.15 | 9.6% | 13.2% | -0.08 |
| Antivirals (year prior to index date) | 8.4% | 38.7% | -0.44 | 21.3% | 48.9% | -0.33 | 12.5% | 37.5% | -0.35 | 21.6% | 15.4% | 0.10 |
| Antivirals (30 days prior to index date) | 3.1% | 33.3% | -0.50 | 17.7% | 47.8% | -0.37 | 7.1% | 34.8% | -0.43 | 15.3% | 15.4% | 0.00 |
| Antivirals (on index date) | 2.2% | 32.1% | -0.51 | 15.6% | 46.7% | -0.39 | 5.2% | 31.3% | -0.43 | 14.4% | 15.4% | -0.02 |
| Beta blocking agents (year prior to index date) | 23.4% | 28.0% | -0.06 | 17.7% | 15.6% | 0.04 | 44.4% | 47.6% | -0.03 | 6.9% | 1.8% | 0.17 |
| Beta blocking agents (30 days prior to index date) | 12.1% | 23.8% | -0.19 | 11.3% | 9.4% | 0.04 | 36.0% | 39.6% | -0.04 | 3.8% | 1.8% | 0.08 |
| Beta blocking agents (on index date) | 9.3% | 23.2% | -0.24 | 11.3% | 9.1% | 0.05 | 31.0% | 38.7% | -0.09 | 3.0% | 1.8% | 0.05 |
| Calcium channel blockers (year prior to index date) | 21.3% | 20.8% | 0.01 | 14.2% | 9.8% | 0.09 | 35.0% | 28.2% | 0.09 | 10.7% | 3.7% | 0.19 |
| Calcium channel blockers (30 days prior to index date) | 11.8% | 16.7% | -0.09 | 8.5% | 5.4% | 0.08 | 27.0% | 22.2% | 0.07 | 8.6% | 3.7% | 0.14 |
| Drug Class                                      | Year Prior to Index Date | 30 Days Prior to Index Date | Index Date       |
|------------------------------------------------|--------------------------|-----------------------------|-----------------|
| Calcium channel blockers                       | 9.8%                     | 14.9%                       | 7.8%            |
| Diuretics                                      | 23.8%                    | 33.9%                       | 19.9%           |
| Drugs for acid related disorders               | 32.9%                    | 57.7%                       | 36.2%           |
| Insulins and analogues                         | 17.2%                    | 25.0%                       | 15.6%           |
| Lipid modifying agents                         | 27.8%                    | 31.0%                       | 18.4%           |
| Immunosuppressants                             | 5.3%                     | 10.1%                       | 13.5%           |
| Drugs for acid related disorders (year prior   | 16.6%                    | 47.0%                       | 28.4%           |
| Drugs for acid related disorders (30 days      | 13.1%                    | 43.5%                       | 26.2%           |
| Immunosuppressants                             | 3.3%                     | 9.5%                        | 9.9%            |
| Insulins and analogues (year prior to index    | 2.7%                     | 9.5%                        | 9.9%            |
| Insulins and analogues (30 days prior to index | 11.1%                    | 19.0%                       | 12.8%           |
| Insulins and analogues (on index date)         | 9.8%                     | 17.3%                       | 12.8%           |
| Lipid modifying agents (year prior to index    | 14.7%                    | 28.0%                       | 13.5%           |
| Lipid modifying agents (30 days prior to index | 10.4%                    | 25.0%                       | 12.8%           |
CUIMC: Columbia University Irving Medical Center; STARR-OMOP: STAnford Medicine Research data Repository; VA OMOP: Department of Veterans Affairs; HIRA: Health Insurance Review & Assessment. COPD: Chronic obstructive pulmonary disease; GERD: Gastroesophageal reflux disease. Exact proportions have not been reported where counts were less than 10.