**Supplemental Table 1: Comprehensive and Ternary Categories of COVID-Relevance to Hospitalization for Manual Chart Review Validation of Candidate Definitions with Case Examples**

|  |  |  |  |
| --- | --- | --- | --- |
| **3-Level Category** | **6-Level Category** | **Description** | **Example** |
| **Primary COVID Hospitalization** | Category 1: Primary  (n=45) | COVID positive on admission, admitted for a syndrome definitely or probably due to COVID infection (e.g. COVID pneumonia, COVID myocarditis, COVID-related multi-system inflammatory syndrome [MIS]) | An elderly man with remote history of tobacco use presented with worsening shortness of breath and cough two weeks after testing positive for SARS-CoV-2 as an outpatient. PCR positive in Emergency Department (ED). A chest-x-ray (CXR) showed bilateral infiltrates consistent with COVID pneumonia. CT angiogram was negative for pulmonary embolism and showed patchy ground glass opacities. Influenza and RSV assays were negative. Oxygen saturation was in low 90s at rest, to high 80s with movement. Admitted, required 1-2L oxygen by low flow nasal cannula. Received remdesivir and dexamethasone. Improved, weaned to room air, and discharged home. |
| An elderly man with history of atrial fibrillation not on anti-coagulation and chronic kidney disease presented with shortness of breath and hypoxemia. Developed chills, fatigue, and cough about one week prior; tested positive for COVID-19 on home rapid antigen test about 5 days before presentation and again in the ED by PCR. Patient required intubation in the ED for severe hypoxemia and respiratory distress and was admitted to the ICU. His gas exchanged improved within days but he suffered several complications, including an MCA stroke, acute on chronic renal failure requiring renal replacement therapy, and ventricular arrhythmias. A do not resuscitate order was placed per family and previously stated patient wishes and he expired. |
| **Contributing COVID Hospitalization** | Category 2: COVID-triggered  (n=16) | COVID positive on admission, admitted for a syndrome potentially related to or triggered by COVID (e.g. CHF exacerbation, arrhythmia, acute myocardial infarction, etc) | An elderly man with a history of progressive cerebellar degenerative disorder followed by Neurology presented with 4 days of worsening dizziness, multiple falls, and frequent headaches. Symptoms were similar to his chronic neurologic complaints but had been acutely worse. Neuro-imaging was unremarkable. Neurology and physical therapy were consulted and the patient was placed in observation. Routine screening PCR for COVID-19 was positive with cycle threshold 38.8. He denied typical COVID symptoms including no fever, chills, cough, shortness of breath. On initial consult, Neurology documented that they felt his presentation was consistent with worsening of his chronic condition; however, after the positive PCR for SARS-CoV-2, the attending attestation documents that COVID/viral infection was a likely contributor. He was discharged home. Per outpatient notes, his neurologic symptoms improved over the following week, more consistent with an acute infection than worsening of his degenerative condition. A close household member also experienced signs/symptoms potentially consistent with COVID-19 though they were not tested. |
| Category 3: Complicates Stay  (n=1), cat 4 | COVID positive on admission, incidental/ not relevant to syndrome or reason for admission, complicates hospitalization (e.g. prolongs stay, causes ICU transfer, causes death; non-medical infection-related discharge challenges such as unable to go to rehab until negative PCR not included as COVID complications) | An elderly man with multiple chronic medical conditions presented after a mechanical fall with a broken hip. Routine screening PCR was positive for SARS-CoV-2. He was mildly hypoxemic on presentation (low 90s on room air) but otherwise asymptomatic. He underwent arthroplasty. Post-operatively he developed fevers and a persistent oxygen requirement of 1-3L. Infectious Diseases felt this was likely due to COVID-19 and recommended hydroxychloroquine. Also treated with empiric antibiotics for 5 days for community acquired pneumonia, though imaging and labs more consistent with viral pneumonia than bacterial pneumonia. Discharged to rehab days later than expected based upon ortho indications alone. |
| Category 4: Late or Nosocomial  (n=0) | COVID positive >2 days after admission, admitted for unrelated reason, complicates hospitalization (e.g. prolongs stay, causes ICU transfer, causes death) | N/A |
| **Incidental COVID Hospitalization** | Category 5: Incidental, Present on Admission  (n=31) cat 3 | COVID positive on admission, incidental/ not relevant to syndrome or reason for admission OR false positive/residual RNA, no complications or impact on hospitalization | An elderly man with diabetes mellitus type 2, coronary artery disease, and chronic kidney disease presented from his nursing home with symptomatic hypoglycemia which improved with glucose infusion in the ED but required admission for observation. Routine COVID-19 PCR was positive (cycle threshold not available). Patient had a documented mild COVID infection one month prior with positive PCR for SARS-CoV-2 at his nursing home and recovered completely in the interim. He had no ongoing symptoms of COVID-19 or need for oxygen supplementation. His presentation was deemed related to ongoing use of sulfonylureas for his diabetes despite his outpatient physician discontinuing them due to renal dysfunction. He was discharged to his nursing home. |
| Category 6: Incidental, Not Present on Admission  (n=7) cat 5 | COVID positive >2 days after admission, admitted for unrelated reason, incidental or false positive/residual RNA, no complications or impact on hospitalization | A middle aged woman without known medical problems presented with 3 days of thumb pain and worsening hand redness and pain after cutting her thumb with a metal scrubbing sponge. She was admitted by Plastic Surgery and treated with IV antibiotics with improvement. Routine SARS-CoV-2 PCR on admission was negative; the test was repeated five days later for new fevers, chills, and malaise and found to be SARS-CoV-2 positive with cycle threshold <20. Discharged home on day of positive test and was not readmitted. |

**Supplemental Table 2. Performance of Candidate Definitions vs Manual Chart Review for COVID Primary/Contributing Hospitalization in Pre-Omicron and Omicron Time Periods**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre-Omicron | | | | | Omicron | | | | | | |
|  | Sens | Spec | ROC | PPV | NPV | | Sens | Spec | ROC | PPV | | NPV |
| PCR only | -\* | -\* | -\* | 76.0 | -\* | | -\* | -\* | -\* | | 48.0 | -\* |
| PCR + hypoxemia | 79.0 | 16.7 | 0.48 (0.35-0.61) | 75.0 | 20.0 | | 79.2 | 42.3 | 0.61 (0.48-0.73) | | 55.9 | 68.8 |
| PCR + dexamethasone | 26.3 | 91.7 | 0.59 (0.48-0.70) | 90.9 | 28.2 | | 50 | 92.3 | 0.71 (0.60-0.83) | | 85.7 | 66.7 |
| PCR + remdesivir | 42.1 | 91.7 | 0.67 (0.55-0.78) | 94.1 | 33.3 | | 83.3 | 88.5 | 0.86 (0.76-0.96) | | 87.0 | 85.2 |
| Institutional COVID-19 flag | 100 | 16.7 | 0.58 (0.47-0.69) | 79.2 | 100 | | 95.8 | 30.8 | 0.63 (0.53-0.73) | | 56.1 | 88.9 |
| ICD-10 | 100 | 33.3 | 0.67 (0.53-0.81) | 82.6 | 100 | | 95.8 | 42.3 | 0.69 (0.59-0.80) | | 60.5 | 91.7 |

\*Sensitivity, specificity, ROC, and NPV were not calculated for Definition 1 as all reviewed cases met PCR-only criteria

**Supplemental Table 3. Sensitivity Analysis Excluding Early Encounters (before November 1, 2020): Incidence of COVID Hospitalization, ICU admission, Mechanical Ventilation, and In-Hospital Mortality in Omicron vs Pre-Omicron Periods for Six Definitions of COVID Hospitalization**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | | **Pre-Omicron** | | **Omicron** | | **Comparison** |
| n | Incidence\* | n | Incidence\* | IRR (95% CI) |
| **COVID Hospitalization** | |  |  |  |  |  |
|  | PCR only | 7,230 | 3.98 | 3,424 | 11.31 | 2.84 (2.73-2.96) |
|  | PCR + hypoxemia | 5,672 | 3.12 | 2,323 | 7.67 | 2.46 (2.34-2.58) |
|  | PCR + dexamethasone | 3,142 | 1.73 | 1,066 | 3.52 | 2.04 (1.90-2.18) |
|  | PCR + remdesivir | 3,548 | 1.95 | 1,496 | 4.94 | 2.53 (2.38-2.69) |
|  | COVID flag | 7,519 | 4.14 | 3,585 | 11.84 | 2.86 (2.75-2.98) |
|  | ICD-10 code for COVID | 7,710 | 4.25 | 3,310 | 10.93 | 2.57 (2.47-2.68) |
| **ICU Admission** | |  |  |  |  |  |
|  | PCR only | 1405 | 19.43 | 467 | 13.64 | 0.70 (0.63-0.78) |
|  | PCR + hypoxemia | 1381 | 24.35 | 448 | 19.29 | 0.79 (0.71-0.88) |
|  | PCR + dexamethasone | 949 | 30.20 | 268 | 25.14 | 0.83 (0.72-0.95) |
|  | PCR + remdesivir | 895 | 25.23 | 294 | 19.65 | 0.78 (0.68-0.89) |
|  | COVID flag | 895 | 18.62 | 434 | 12.11 | 0.65 (0.58-0.72) |
|  | ICD-10 code for COVID | 1400 | 19.18 | 450 | 13.60 | 0.71 (0.63-0.79) |
| **Mechanical Ventilation** | |  |  |  |  |  |
|  | PCR only | 988 | 13.67 | 320 | 9.35 | 0.68 (0.60-0.78) |
|  | PCR + hypoxemia | 988 | 17.42 | 320 | 13.78 | 0.79 (0.70-0.90 |
|  | PCR + dexamethasone | 684 | 21.77 | 194 | 18.20 | 0.84 (0.71-0.98) |
|  | PCR + remdesivir | 628 | 17.70 | 205 | 13.70 | 0.77 (0.66-0.91) |
|  | COVID flag | 963 | 12.81 | 303 | 8.45 | 0.66 (0.58-0.75) |
|  | ICD-10 code for COVID | 1025 | 13.29 | 210 | 6.34 | 0.70 (0.62-0.80) |
| **In-Hospital Mortality** | |  |  |  |  |  |
|  | PCR only | 631 | 8.73 | 193 | 5.64 | 0.85 (0.73-0.98) |
|  | PCR + hypoxemia | 620 | 10.93 | 191 | 8.22 | 0.96 (0.83-1.11) |
|  | PCR + dexamethasone | 422 | 13.43 | 127 | 11.91 | 1.03 (0.85-1.24) |
|  | PCR + remdesivir | 350 | 9.86 | 125 | 8.36 | 1.05 (0.87-1.27) |
|  | COVID flag | 712 | 20.07 | 202 | 5.63 | 0.75 (0.65-0.87) |
|  | ICD-10 code for COVID | 700 | 9.31 | 210 | 6.34 | 0.87 (0.75-1.00) |

\*For COVID Hospitalization, incidence is the number of COVID cases per 100 encounters; for ICU admission, Mechanical Ventilation, and In-Hospital Mortality, incidence is the number of outcome cases per 100 COVID encounters based on given definition.