**Additional File 1**

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**Supplementary Figure 1**

**Hospitalization according to Hydroxychloroquine Exposure from Self-Reported Onset of COVID-19 Symptoms**



**Cumulative prevalence of hospitalization among mildly symptomatic COVID-19 patients according to outpatient exposure to hydroxychloroquine from onset of self-reported symptoms**

**HCQ=hydroxychloroquine.**

Supplementary Table 1

**Matched multivariate logistic regression model with the stepwise (AIC based) variable selection procedure for hospitalization (sample size=1067)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.546 | (0.3,0.96) | 0.040 |
| Age | 1.024 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.373 | (1.00,1.88) | 0.047 |
| COPD/Asthma, yes/no | 0.682 | (0.43,1.07) | 0.096 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Shortness of Breath, yes/no | 6.309 | (4.59,8.74) | <0.001 |
| **Disease severity,**  **n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.187 | (0.14,0.26) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.344 (g=8)

Supplementary Table 1 – missing data excluded

**Matched multivariate logistic regression model with the stepwise (AIC based) variable selection procedure hospitalization excluding individuals with any missing values. (sample size=993)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.527 | (0.29,0.94) | 0.033 |
| Age | 1.023 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.281 | (0.93,1.76) | 0.125 |
| COPD/Asthma, yes/no | 0.673 | (0.43,1.05) | 0.087 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Shortness of Breath, yes/no | 6.219 | (4.51,8.64) | <0.001 |
| **Disease severity,**  **n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.193 | (0.14,0.27) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.708 (g=8)

Supplementary Table 2

**Matched regression model with variables selected by Lasso (sample size=1067)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.544 | (0.30,0.96) | 0.039 |
| Age | 1.023 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.34 | (0.98,1.84) | 0.069 |
| Diabetes, yes/no | 1.227 | (0.82,1.82) | 0.314 |
| COPD/Asthma, yes/no | 0.709 | (0.45,1.11) | 0.138 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.196 | (0.85,1.69) | 0.31 |
| Shortness of Breath, yes/no | 5.961 | (4.28,8.38) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.188 | (0.14,0.26) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.444 (g=10)

Supplementary Table 2 – missing data excluded

**Matched regression model with variables selected by Lasso excluding individuals with any missing values. (sample size=993)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.524 | (0.28,0.93) | 0.032 |
| Age | 1.023 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.23 | (0.89,1.69) | 0.206 |
| Diabetes, yes/no | 1.237 | (0.83,1.84) | 0.297 |
| COPD/Asthma, yes/no | 0.7 | (0.44,1.10) | 0.127 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.303 | (0.89,1.91) | 0.174 |
| Cough, yes/no | 0.818 | (0.55,1.22) | 0.323 |
| Shortness of Breath, yes/no | 6.18 | (4.35,8.88) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.195 | (0.14,0.27) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.145 (g=11)

Supplementary Table 3

**Unmatched multivariable logistic regression model for hospitalization (sample size=1274)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Multivariable adjusted** | | | **Unadjusted** | | |
|  | **Estimated OR** | **OR 95% CI** | **P value** | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.533 | (0.29,0.94) | 0.034 | 0.653 | (0.39,1.06) | 0.094 |
| Age | 1.02 | (1.01,1.03) | <0.001 | 1.019 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.361 | (1.01,1.83) | 0.042 | 1.445 | (1.13,1.84) | 0.003 |
| Diabetes, yes/no | 1.255 | (0.84,1.87) | 0.262 | 1.551 | (1.13,2.13) | 0.007 |
| Hypertension yes/no | 0.959 | (0.67,1.37) | 0.817 | 1.212 | (0.94,1.56) | 0.138 |
| COPD/Asthma, yes/no | 0.73 | (0.47,1.13) | 0.162 | 1.019 | (0.71,1.45) | 0.917 |
| Cancer, yes/no | 1.022 | (0.60,1.72) | 0.934 | 1.269 | (0.84,1.91) | 0.256 |
| **Presenting Symptoms, n (%)** |  |  |  |  |  |  |
| Fever, yes/no | 1.274 | (0.90,1.80) | 0.167 | 2.174 | (1.69,2.80) | <0.001 |
| Cough, yes/no | 0.847 | (0.59,1.22) | 0.371 | 1.981 | (1.54,2.55) | <0.001 |
| Shortness of Breath, yes/no | 5.707 | (4.13,7.96) | <0.001 | 6.171 | (4.75,8.05) | <0.001 |
| **Disease severity, n (%)** |  |  |  |  |  |  |
| qSOFA Score, 1/0 | 0.19 | (0.14,0.26) | <0.001 | 0.159 | (0.12,0.21) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.436 (g=13) ) for the multivariate logistic regression model. Neutrophil / Lymphocyte was not used due to its high missing frequency (70%).

**Unmatched multivariable logistic regression model for hospitalization excluding individuals with any missing values. (sample size=1077)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.51 | (0.28,0.91) | 0.026 |
| Age | 1.021 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.265 | (0.94,1.71) | 0.125 |
| Diabetes, yes/no | 1.246 | (0.83,1.86) | 0.281 |
| Hypertension yes/no | 0.938 | (0.66,1.34) | 0.728 |
| COPD/Asthma, yes/no | 0.713 | (0.45,1.11) | 0.137 |
| Cancer, yes/no | 1.08 | (0.64,1.82) | 0.775 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.287 | (0.91,1.82) | 0.156 |
| Cough, yes/no | 0.843 | (0.58,1.22) | 0.366 |
| Shortness of Breath, yes/no | 5.63 | (4.06,7.87) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.202 | (0.149,0.27) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.375 (g=13) ) for the multivariate logistic regression model.

Supplementary Table 4

**Unmatched multivariable logistic regression model with the stepwise (AIC based) variable selection procedure for hospitalization (sample size=1274)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.552 | (0.31,0.96) | 0.042 |
| Age | 1.021 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.4 | (1.04,1.88) | 0.025 |
| COPD/Asthma, yes/no | 0.695 | (0.45,1.07) | 0.103 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Shortness of Breath, yes/no | 5.827 | (4.33,7.90) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.186 | (0.14,0.25) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.193 (g=8)

Supplementary Table 4 – missing data excluded

**Unmatched multivariable logistic regression model with the stepwise (AIC based) variable selection procedure for hospitalization excluding individuals with any missing values. (sample size=1077)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.523 | (0.29,0.92) | 0.029 |
| Age | 1.021 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.298 | (0.96,1.75) | 0.086 |
| COPD/Asthma, yes/no | 0.693 | (0.44,1.07) | 0.104 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Shortness of Breath, yes/no | 5.700 | (4.21,7.76) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.200 | (0.15,0.27) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.269 (g=8)

Supplementary Table 5

**Unmatched multivariable regression model with variables selected by Lasso (sample size=1274)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.536 | (0.30,0.94) | 0.033 |
| Age | 1.02 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.361 | (1.01,1.83) | 0.042 |
| Diabetes, yes/no | 1.246 | (0.85,1.82) | 0.259 |
| COPD/Asthma, yes/no | 0.729 | (0.47,1.13) | 0.159 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.28 | (0.91,1.81) | 0.159 |
| Cough, yes/no | 0.855 | (0.59,1.23) | 0.397 |
| Shortness of Breath, yes/no | 5.759 | (4.17,8.02) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.188 | (0.14,0.25) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.156 (g=11)

Supplementary Table 5 – missing data excluded

**Unmatched multivariable regression model with variables selected by Lasso excluding individuals with any missing values. (sample size=1077)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.515 | (0.28,0.91) | 0.026 |
| Age | 1.02 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.267 | (0.94,1.71) | 0.123 |
| Diabetes, yes/no | 1.221 | (0.83,1.79) | 0.308 |
| COPD/Asthma, yes/no | 0.711 | (0.45,1.10) | 0.133 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.288 | (0.91,1.83) | 0.153 |
| Cough, yes/no | 0.843 | (0.58,1.22) | 0.364 |
| Shortness of Breath, yes/no | 5.647 | (4.08,7.89) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.201 | (0.15,0.27) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.446 (g=11)

Supplementary Table 6

**Unmatched multivariable logistic regression model with PS score for hospitalization (sample size=1274)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.532 | (0.29,0.94) | 0.034 |
| Age | 1.02 | (1.01,1.03) | <0.001 |
| Gender, male/female | 1.204 | (0.73,1.94) | 0.456 |
| Diabetes, yes/no | 1.26 | (0.85,1.87) | 0.255 |
| Hypertension yes/no | 1.017 | (0.68,1.52) | 0.936 |
| COPD/Asthma, yes/no | 0.802 | (0.47,1.36) | 0.417 |
| Cancer, yes/no | 1.835 | (0.29,13.31) | 0.536 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.481 | (0.84,2.7) | 0.191 |
| Cough, yes/no | 0.792 | (0.52,1.20) | 0.279 |
| Shortness of Breath, yes/no | 5.738 | (4.15,8.00) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.219 | (0.13,0.38) | <0.001 |
| PS score | 0.005 | (0,39274.80) | 0.537 |

Note : Test of model goodness of fit shows a good fit with p-value=0.250 (g=11)

Supplementary Table 7

**Multivariable logistic regression model for hospitalization in symptomatic subgroup (sample size=749)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.743 | (0.39,1.37) | 0.355 |
| Age | 1.038 | (1.03,1.05) | <0.001 |
| Gender, male/female | 1.595 | (1.13,2.26) | 0.008 |
| Diabetes, yes/no | 1.562 | (0.99,2.48) | 0.057 |
| Hypertension yes/no | 0.756 | (0.50,1.13) | 0.178 |
| COPD/Asthma, yes/no | 0.951 | (0.59,1.53) | 0.836 |
| Cancer, yes/no | 1.151 | (0.63,2.09) | 0.643 |
| **Disease severity,**  **n (%)** |  |  |  |
| qSOFA Score, 1/0 | 0.184 | (0.13,0.26) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.339 (g=10)

Supplementary Figure 2

**Hospitalization according to Hydroxychloroquine Exposure Among Cohort with Fever, Cough or Shortness of Breath at Time of Evaluation**



**Cumulative prevalence of hospitalization among mildly symptomatic COVID-19 patients who self-report at least fever, cough or shortness of breath at time of evaluation according to outpatient exposure to hydroxychloroquine. HCQ=hydroxychloroquine.**

Supplementary Table 8

A) Matched multivariable logistic regression model for hospitalization in age subgroup (sample size=282)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.489 | (0.17,1.32) | 0.171 |
| Gender, male/female | 0.919 | (0.50,1.69) | 0.786 |
| Diabetes, yes/no | 1.153 | (0.58,2.30) | 0.686 |
| Hypertension yes/no | 0.744 | (0.37,1.48) | 0.4 |
| COPD/Asthma, yes/no | 1.016 | (0.45,2.25) | 0.968 |
| Cancer, yes/no | 0.798 | (0.36,1.76) | 0.578 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Fever, yes/no | 1.17 | (0.57,2.37) | 0.663 |
| Cough, yes/no | 1.003 | (0.47,2.08) | 0.994 |
| Shortness of Breath, yes/no | 11.298 | (5.68,23.84) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| SOFA Score, 1/0 | 0.187 | (0.10,0.35) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.622 (g=12)

B) Matched multivariate logistic regression model with the stepwise (AIC based) variable selection procedure for hospitalization in age subgroup(sample size=282)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.424 | (0.15,1.10) | 0.087 |
| Diabetes, yes/no | 1.122 | (0.58,2.18) | 0.734 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Shortness of Breath, yes/no | 11.544 | (6.26,22.27) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| SOFA Score, 1/0 | 0.192 | (0.10,0.35) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.865 (g=6)

C) Matched regression model with variables selected by Lasso in age subgroup (sample size=282)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| HCQ, yes/no | 0.423 | (0.15,1.11) | 0.088 |
| **Presenting Symptoms, n (%)** |  |  |  |
| Shortness of Breath, yes/no | 10.267 | (5.67,19.27) | <0.001 |
| **Disease severity, n (%)** |  |  |  |
| SOFA Score, 1/0 | 0.198 | (0.11,0.36) | <0.001 |

Note : Test of model goodness of fit shows a good fit with p-value=0.700 (g=5)

Supplementary Table 9

Univariate logistic regression in HCQ subgroup with symptoms (sample size=69)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimated OR** | **OR 95% CI** | **P value** |
| Days From symptom onset to TRT, >2/<=2 | 3.429 | (0.57,66.01) | 0.262 |