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Brief report

# Association between Influenza Vaccination and severe COVID-19 outcomes at a designated COVID-only hospital in Brooklyn



Ogie Q. Umasabor-Bubu MD MPH <sup>a,b,1,\*</sup>, Omonigho M. Bubu MD MPH PhD <sup>c,d</sup>, Alfred K. Mbah PhD <sup>e</sup>, Mohamed Nakeshbandi MD <sup>b</sup>, Tonya N. Taylor PhD <sup>f</sup>

<sup>a</sup> Department of Epidemiology and Infection Control, State University New York Downstate Medical Center, Brooklyn, NY

<sup>b</sup> Department of Medicine, Division of Infectious Disease, State University of New York, Downstate Health Sciences University, Brooklyn, NY

<sup>c</sup> Center for Healthful Behavior Change, Department of Population Health, NYU Grossman School of Medicine, New York, NY

<sup>d</sup> Center for Sleep and Brain Health, Department of Psychiatry, NYU Grossman School of Medicine, New York, NY

<sup>e</sup> Department of Epidemiology and Biostatistics, College of Public Health, University of South Florida, Tampa, FL

<sup>f</sup> Department of Medicine, Division of Infectious Disease, Special Treatment and Research (STAR) Program, SUNY Downstate Health Sciences University, Brooklyn, NY

Key Words: Influenza Vaccination COVID-19 Coronavirus COVID-19 mortality COVID-19 severity

#### ABSTRACT

Maintaining influenza vaccination at high coverage has the potential to prevent a proportion of COVID-19 morbidity and mortality. We examined whether flu-vaccination is associated with severe corona virus disease 2019 (COVID-19) disease, as measured by intensive care unit (ICU)-admission, ventilator-use, and mortality. Other outcome measures included hospital length of stay and total ICU days. Our findings showed that flu-vaccination was associated with a significantly reduced likelihood of an ICU admission especially among aged <65 and non-obese patients. Public health promotion of flu-vaccination may help mitigate the overwhelming demand for critical COVID-19 care pending the large-scale availability of COVID-19 vaccines.

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Author contributions: All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. OQB, OMB, TT: Concept and design; OQB, TT: Data Acquisition; OQB, OMB, AKM, TT: Analysis or interpretation of data; OQB, TT: Drafting of the manuscript. Critical revision of the manuscript for important intellectual content: All authors. AKM, OMB: Statistical analysis; MN, OQB, OMB, AKM: Administrative, technical, or material support; MN, TT: Supervision

<sup>1</sup> These authors contributed equally (Umasabor-Bubu OQ, Bubu OM)

In the United States, the Coronavirus disease-2019 (COVID-19) pandemic has resulted in 31.3 million confirmed cases and over 562,000 deaths as of April 13, 2021.<sup>1</sup> Experts had warned of a possible second wave in late fall and winter, corresponding with the influenza (flu) season. Influenza co-infection with COVID-19 brings with it challenges of clinically distinguishing both infectious agents, test cross-reactivity and accuracy; and possibly enhancing the risk for severe COVID-19. This can significantly affect downstream public health efforts to properly identify COVID-19 cases and contain the outbreak particularly in resource-limited settings. Flu-vaccination reduces Influenza disease severity and hospitalizations among at-risk populations, such as children, older adults (aged 65>), and pregnant women. Mathematical models suggest that maintaining high influenzavaccination coverage has the potential to significantly reduce the proportion of COVID-19 morbidity and mortality, and the risk of cross-infection.<sup>2,3</sup> Here, we examined whether prior flu-vaccination reduces the likelihood of COVID-19 disease severity, as measured by hospital length of stay, ICU-admission, ICU length of stay, ventilator-use, and in-hospital mortality.

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<sup>\*</sup> Address correspondence to: Ogie Q. Umasabor-Bubu, MD, MPH, CPH CIC, 440 Lenox Road, Brooklyn, NY 11203. Tel.: +1 718 270 4120.

*E-mail addresses*: ogie.umasabor-bubu@downstate.edu (O.Q. Umasabor-Bubu), omonigho.bubu@nyulangone.org (O.M. Bubu).

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# **METHODS**

We conducted a retrospective chart review of 588 COVID-19 hospitalized patients admitted during the height of the pandemic's first wave, between 03/12/2020 and 06/30/2020 at SUNY Downstate Medical Center; a New York State designated COVID-only hospital. Patients reported on admission if they had been previously vaccinated for Influenza (Yes or No) during last flu-season (09/01/19 - 03/ 31/20). SUNY Downstate Medical Center institutional review board approved this study. Dichotomous (Yes or No) outcome measures included whether patients required ICU-admission, mechanical-ventilation or experienced in-hospital mortality. Continuous outcome measures included hospital length of stay defined as total hospital stay days from admission to discharge or death, and ICU length of stay, defined as total ICU stay days from admission to ICU to discharge from ICU or death. COVID-19 diagnosis was confirmed using quantitative reverse transcription-polymerase chain reaction (RT-PCR) assay of nasopharyngeal swabs.

#### Statistical analyses

Descriptive statistics were calculated for demographic and clinical data for the sample. Characteristics of the study groups (self-reported flu vaccination Yes vs No) were compared using Pearson's chi-square test, or Fisher's exact test where appropriate, for categorical variables (eg, sex) and t-test for continuous variables (eg, age). Clinical data comparison between flu-vaccinated groups included use of the Charlson's co-morbidity index scores,<sup>4</sup> to account for multiple comorbidities that could be potentially associated with COVID19 infection. Adjusted multivariate logistic regression analyses quantified the effect of flu-vaccination on the rates of ICU-admission, ventilator-use and mortality (Table 2). Adjusted multivariate linear regression analyses quantified the effect of flu-vaccination on hospital and ICU length of stay. Since individuals who are older than 65 years and those who are obese are more likely to develop severe COVID-19 disease,<sup>5</sup> we also conducted stratified analyses by age (<65 and  $\geq$ 65 y) and BMI (<30 and  $\geq$ 30 kg/  $m^2$ ). Covariates/potential confounders were selected *a priori* and were chosen based on the literature and their clinical relevance to COVID-19

Table 1

Characteristics of all 588 RCT-PCR confirmed COVID-19 positives, between 03/12/20 and 05/30/20 SUNY downstate health sciences medical center, Brooklyn, New York

Femalesce no. (3) Age years mean (3D)     277 (47.1)     179 (46.9)     98 (47.6)     87       Age years mean (3D) Age years mean (3D)     68.4 (14.5)     68.6 (14.1)     68.9 (14.1)     68.9 (14.1)     79       Age years mo. (8)	Clinical characteristics	All patients n = 588	Self-reported flu vaccination - No n = 382	Self-reported flu vaccination -Yes n = 206	P-value
Age years mean (SD)     All Patients     68.4 (14.5)     68.6 (14.1)     68.9 (14.1)     7.9       4ge years no (N)     53.1 (9.1)     7.5.2 (9.8)     53.1 (9.1)     7.5.2 (9.8)     53.1 (9.1)     7.5.2 (9.8)     53.1 (9.1)     7.5.2 (9.8)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7.6.5 (8.4)     7	Female sex no. (%)	277 (47.1)	179 (46.9)	98 (47.6)	.87
All Patients     68 (14.5)     68 (6 (1.4)     69 (9.1,1)     7.9       sep ears no (%)     526     52.7 (9.8)     53.1 (9.1)     52.3 (9.6)     56       Race[Ethnicity no (%)     70.0 (7.9)     76.5 (8.4)     7       Race[Ethnicity no (%)     17 (8.6)     7     7       Africa American     519 (8.8)     23 (60)     17 (8.3)     7       Other     29 (4.9)     18 (4.7)     115.3     7       BM lig/m <sup>2+</sup> mean (5D)     115.3     115.3     8     14 (8.9)     24.8 (3.8)     25.0 (3.6)     24.5 (4.1)     86       S20     23.7 (10.1)     38 (10.2)     35.4 (8.7)     10     10       Co-motibilities no. (%)	Age years mean (SD)				
Age years no. (%)     Subscript     Solution     Solution </td <td>All Patients</td> <td>68.4 (14.5)</td> <td>68.6 (14.1)</td> <td>68.9 (14.1)</td> <td>.79</td>	All Patients	68.4 (14.5)	68.6 (14.1)	68.9 (14.1)	.79
<65	Age years no. (%)				
≥6576.9 (8.1)77.0 (7.9)76.5 (8.4)Arica American519 (88.3)341 (89.3)178 (86.4)7.Arica American519 (88.3)341 (89.3)178 (86.4)7.Non-Hispanic White40 (6.8)22 (60)17.7 (8.3)11 (5.3)BM kg/m <sup>2+</sup> mean (SD)30.3 (9.5)30.8 (10.2)28.9 (8.3)1.4<30	<65	52.7 (9.8)	53.1 (9.1)	52.3 (9.7)	.56
Race/Ethnicity no. (%)     74 (16.0. An merican     519 (88.3)     341 (89.3)     17.8 (86.4)     7.       Non-Hispanic White     40 (6.8)     23 (60)     17 (8.3)     11 (5.3)       BMI kg/m <sup>2+s</sup> mean (SD)     118 (4.7)     11 (5.3)     14       All readers     303 (9.5)     30.8 (10.2)     28.9 (8.3)     .14       All readers     303 (9.5)     30.8 (10.2)     28.9 (8.3)     .14       Sall sig/m <sup>2+s</sup> mean (SD)	≥65	76.9 (8.1)	77.0 (7.9)	76.5 (8.4)	
African American519 (88.3)341 (89.3)178 (86.4)7.Non-Hispanic White40 (6.8)23 (60)17 (8.3)Other29 (4.9)18 (4.7)11 (5.3)BMI kg/m <sup>2+</sup> mea (5D)30.8 (10.2)28.9 (8.3).14-3024.8 (3.8)25.0 (3.6)24.5 (4.1).86 $\geq 30$ 37.7 (10.1)38.8 (10.9)35.4 (8.7)Co-morbidities no. (3)467 (79.4)298 (78.0)169 (82.0).31Diabetes311 (52.9)209 (54.7)102 (49.5).22Hypertension467 (79.4)298 (78.0)169 (82.0)Diabetes311 (52.9)209 (54.7)102 (49.5)Cor-morbidities no. (3)102 (17.3)66 (17.3)36 (17.5)Chronic Kidney disease102 (17.3)66 (17.3)36 (17.5)COPD47 (8.0)27 (7.1)20 (9.7).18Chronic Kidney disease79 (13.4)53 (13.9)24 (11.7).15Astima45 (7.7)32 (8.4)13 (6.3)Astima'45 (7.7)32 (8.4)13 (6.3)Amina'45 (7.7)32 (8.4)13 (6.3)Astima'206 (55.0)318 (83.2)187 (90.7)<.01	Race/Ethnicity no. (%)				
Non-Hispanic White     40 (6.8)     23 (60)     17 (5.3)       Other     29 (49)     18 (4.7)     11(5.3)       BMI kg/m <sup>2+</sup> mean (SD)     1     1     1       All Patients     30.3 (9.5)     28.0 (8.3)     2.4       BMI kg/m <sup>2+</sup> mo. (%)     2     2     2.5 (0.3.6)     2.4 5 (4.1)     .86       230     3.7 (10.1)     28.8 (10.9)     3.5 (8.7)     .22       Hypertension     467 (79.4)     2.98 (78.0)     169 (82.0)     .31       Diabetes     3.11 (52.9)     2.09 (54.7)     102 (49.5)     .22       Hypertingidemia     205 (34.9)     135 (53.3)     70 (34.0)     .55       coronary artery disease     102 (17.3)     66 (77.3)     36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     2.3 (11.2)     .23     .23       COPD     47 (8.0)     27 (1.3)     .51 (13.9)     .24 (11.7)     .15       Asthma     45 (7.7)     32 (8.4)     .13 (6.3)     .32     .32       Malignant tumor     32 (5.4)     .24 (0.11)	African American	519 (88.3)	341 (89.3)	178 (86.4)	.7
Other     29 (49)     18 (4.7)     11 (5.3)       MI kg/m <sup>**</sup> mean (5D)	Non-Hispanic White	40 (6.8)	23 (60)	17 (8.3)	
BMI kg/m <sup>2+</sup> mean (SD)     BMI kg/m <sup>2+</sup> mo. (%)     AII Patients     30.3 (9.5)     30.8 (10.2)     28.9 (8.3)     1.4       BMI kg/m <sup>2+</sup> mo. (%)     25.0 (3.6)     24.5 (4.1)     .86       2-30     37.7 (10.1)     38.8 (10.9)     35.4 (8.7)       Co-morbidities no. (%)       .71       Hypertension     467 (79.4)     298 (78.0)     169 (82.0)     .31       Diabetes     311 (52.9)     200 (54.7)     102 (49.5)     .22       Hypertipidemia     205 (34.9)     135 (35.3)     70 (34.0)     .55       coronary artery disease     102 (17.3)     66 (17.3)     36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     .23 (11.2)     .23       chronic kidney disease     79 (13.4)     52 (13.6)     .27 (13.1)     .57       ESRD     77 (13.1)     53 (13.9)     .24 (11.7)     .15       Asthma     45 (7.7)     32 (84.1)     13 (6.3)     .32       Malignant tumor     32 (5.4)     20 (0.1)     .20 (0.13)     .68       Symptoms/signs no. (%) <td< td=""><td>Other</td><td>29 (4.9)</td><td>18 (4.7)</td><td>11(5.3)</td><td></td></td<>	Other	29 (4.9)	18 (4.7)	11(5.3)	
All Patients   303 (9.5)   308 (10.2)   28.9 (8.3)   1.4     BM lkg/m <sup>2</sup> n.0. (%)   24.8 (3.8)   25.0 (3.6)   24.5 (4.1)   .86     ≥30   24.8 (3.8)   25.0 (3.6)   24.5 (4.1)   .86     ≥30   37.7 (10.1)   38.8 (10.9)   35.4 (8.7)   .7     Co-morbidities no. (%)	BMI kg/m <sup>2**</sup> mean (SD)				
BMI kg/m <sup>2*</sup> no. (%)   36   248 (3.8)   25.0 (3.6)   24.5 (4.1)   86     ≥30   37.7 (10.1)   38.8 (10.9)   35.4 (8.7)   7     Co-morbidities no. (%)   7   7   9298 (78.0)   166 (82.0)   31     Diabetes   311 (52.9)   209 (54.7)   102 (49.5)   22     Hypertipidemia   205 (34.9)   135 (35.3)   70 (34.0)   55     coronary artery disease   102 (17.3)   66 (17.3)   36 (17.5)   .54     COP   47 (8.0)   27 (7.1)   20 (9.7)   .18     chronic kidney disease   79 (13.4)   53 (13.6)   27 (13.1)   .57     ESRD   77 (13.1)   53 (13.6)   22 (11.7)   .15     Asthma   45 (7.7)   32 (8.4)   13 (63.3)   .32     Malignant tumor   32 (54)   22 (0.01.1)   2.0 (0.13)   .69     Symptoms/signs no. (%)   W   83 (75.5)   303 (79.3)   147 (71.0)   .60     Cough   450 (75.5)   303 (79.3)   147 (71.0)   .65   .66   .61     Symptoms/signs no. (%)   Ever   16 (19.7)	All Patients	30.3 (9.5)	30.8 (10.2)	28.9 (8.3)	.14
-30     248 (.8)     250 (.36)     245 (4.1)     .86       >20     37.7 (10.1)     38.8 (10.9)     35.4 (8.7)       Co-morbidities no. (%)       169 (82.0)     .31       Diabetes     311 (52.9)     209 (54.7)     102 (49.5)     .22       Hyperlipidemia     205 (34.9)     135 (35.3)     .70 (34.0)     .55       coronary artery disease     102 (17.3)     .66 (17.3)     .36 (17.5)     .54       CVP)/Stoke     .65 (11.1)     .42 (11.0)     .23 (11.2)     .23       COPD     .47 (8.0)     .27 (7.1)     .20 (9.7)     .18       drionic kidney disease     .79 (13.1)     .53 (13.9)     .24 (11.7)     .15       Asthma     .45 (7.7)     .32 (8.4)     .13 (6.3)     .32       Malignant tumor     .32 (5.4)     .22 (5.8)     .10 (4.9)     .44       Corgh     .45 (07.5)     .33 (7.9)     .47 (13.1)     .55       Symptoms/signs no.(%)	BMI kg/m <sup>2**</sup> no. (%)				
≥30     37.7 (10.1)     38.8 (10.9)     35.4 (8.7)       Co-morbidities no.(%)           Hypertension     467 (79.4)     298 (78.0)     169 (82.0)     .31       Diabetes     311 (52.9)     209 (54.7)     102 (49.5)     .22       Hyperlipidemia     205 (34.9)     135 (35.3)     70 (34.0)     .55       coronary artery disease     102 (17.3)     66 (17.3)     36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     23 (11.2)     .23       COPD     47 (8.0)     27 (7.1)     20 (9.7)     .18       chronic kidney disease     79 (13.4)     52 (13.6)     27 (13.1)     .57       ESRD     77 (13.1)     53 (18.9)     24 (11.7)     .15       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlsor's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.13)     .67     .55       SymptomSigins no. (%)      16     .50	<30	24.8 (3.8)	25.0 (3.6)	24.5 (4.1)	.86
Co-mobidities no.(%)     31       Hypertension     467 (79.4)     298 (78.0)     169 (82.0)     .31       Diabetes     311 (52.9)     209 (54.7)     102 (49.5)     .22       Hyperlipidemia     205 (34.9)     135 (35.3)     70 (34.0)     .55       coronary attery disease     102 (17.3)     66 (17.3)     .36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     .23 (11.2)     .23       CVD/Stroke     79 (13.4)     .52 (13.6)     .27 (13.1)     .57       ESRD     77 (13.1)     .53 (13.9)     .24 (11.7)     .15       Asthma     45 (7.7)     .22 (8.4)     .13 (6.3)     .32       Malignant tumor     .32 (5.4)     .22 (5.8)     .10 (4.9)     .44       Charlos comorbidity index mean (SD)     .20 (0.1)     .20 (0.1)     .20     .55       Symptoms/signs no.(%)     F     Fever     .50 (85.9)     .318 (83.2)     .187 (90.7)     <0.1	≥30	37.7 (10.1)	38.8 (10.9)	35.4 (8.7)	
Hypertension     467 (79.4)     288 (78.0)     169 (82.0)     31       Diabetes     311 (52.9)     209 (54.7)     102 (49.5)     .22       Hyperipidemia     205 (34.9)     135 (35.3)     70 (34.0)     .55       coronary artery disease     102 (17.3)     66 (17.3)     36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     23 (11.2)     .23       COPD     47 (8.0)     27 (7.1)     20 (9.7)     .18       chronic kidney disease     79 (13.4)     53 (13.9)     24 (11.7)     .15       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     .20 (0.13)     .69       Symptoms/signs no. (%)     T     T     T     .666.0)     .88       Cough     450 (76.5)     303 (79.3)     147 (71.0)     .65       Dyspnea     400 (68.0)     264 (69.1)     136 (66.0)     .88       Dest Pain	Co-morbidities no. (%)				
Diabetes     311 (52.9)     209 (54.7)     102 (49.5)     22       Hyperlipidemia     205 (34.9)     135 (35.3)     70 (34.0)     .55       coronary artery disease     102 (17.3)     66 (17.3)     36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     23 (11.2)     .23       CVD     47 (8.0)     27 (7.1)     20 (9.7)     .18       Chronic kidney disease     79 (13.4)     53 (13.9)     24 (11.7)     .15       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Symptoms/signs no.(%)     -     -     -     -       Fever     505 (85.9)     18 (83.2)     187 (90.7)     <01	Hypertension	467 (79.4)	298 (78.0)	169 (82.0)	.31
Hyperlipidemia     205 (34.9)     135 (35.3)     70 (34.0)     55       coronary artery disease     102 (17.3)     66 (17.3)     36 (17.5)     .54       CVD/Stroke     65 (11.1)     42 (11.0)     23 (11.2)     .23       COPD     47 (8.0)     27 (7.1)     20 (9.7)     .18       chronic kidney disease     79 (13.4)     53 (13.9)     24 (17.7)     .55       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     2.0 (0.13)     .69       Symptoms/signs no. (%)     r     r     r     r     .450 (76.5)     .303 (79.3)     147 (71.0)     .05       Dyspnea     400 (68.0)     264 (69.1)     136 (66.0)     .08     .99     .99     .99     .91     .91     .91       Respiratory illness     116 (19.7)     76 (19.9)     40 (19.4)     .61     .91     .91     .92     .92     .92     .92	Diabetes	311 (52.9)	209 (54.7)	102 (49.5)	.22
coronary artery disease     102 (17.3)     66 (17.3)     36 (17.5)     54       CVD/Stroke     65 (11.1)     42 (11.0)     23 (11.2)     .23       COPD     47 (8.0)     27 (7.1)     20 (9.7)     .18       chronic kidney disease     79 (13.4)     52 (13.6)     27 (13.1)     .57       ESRD     77 (13.1)     53 (13.9)     24 (11.7)     .15       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     2.0 (0.13)     .69       Symptoms/signs no. (%)     Fever     505 (85.9)     318 (83.2)     187 (90.7)     <.01	Hyperlipidemia	205 (34.9)	135 (35.3)	70 (34.0)	.55
CVD/Stroke     65 (11.1)     42 (11.0)     23 (11.2)     23       COPD     47 (8.0)     27 (7.1)     20 (9.7)     1.8       CND chronic kidney disease     79 (13.4)     52 (13.6)     27 (13.1)     57       ESRD     77 (13.1)     53 (13.9)     24 (11.7)     1.5       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     2.0 (0.13)     .69       Symptoms/signs no.(%)     -     -     -     -     -       Fever     505 (85.9)     318 (83.2)     187 (90.7)     <.01	coronary artery disease	102 (17.3)	66 (17.3)	36(17.5)	.54
COPD     47 (8.0)     27 (7.1)     20 (9.7)     18       chronic kidney disease     79 (13.4)     52 (13.6)     27 (13.1)     5.7       ESRD     77 (13.1)     53 (13.9)     24 (11.7)     1.5       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     2.0 (0.13)     .69       Symptoms/signs no. (%)        .666.0)     .68       Cough     450 (76.5)     303 (79.3)     147 (71.0)     .05       Dyspnea     400 (68.0)     264 (69.1)     136 (66.0)     .08       Chest Pain     206 (35.0)     141 (36.9)     65 (31.6)     .19       Respiratory illness     116 (19.7)     76 (19.9)     40 (19.4)     .61       Anemia     25 (4.3)     18 (47,1)     7 (3.4)     .45       Myalgia     179 (30.4)     111 (29.1)     66 (32)     .46       Diarrhea     120 (32.7)     1	CVD/Stroke	65 (11.1)	42 (11.0)	23 (11.2)	.23
chronic kidney disease     79 (13.4)     52 (13.6)     27 (13.1)     57       ESRD     77 (13.1)     53 (13.9)     24 (11.7)     .15       Asthma     45 (7.7)     32 (8.4)     13 (6.3)     .32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     2.0 (0.13)     .69       Symptoms/signs no. (%)        .67     .61       Fever     505 (85.9)     318 (83.2)     187 (90.7)     .61       Cough     450 (76.5)     303 (79.3)     147 (71.0)     .05       Dyspnea     400 (68.0)     264 (69.1)     136 (66.0)     .08       Chest Pain     206 (35.0)     141 (36.9)     65 (31.6)     .19       Pneumonia     119 (20.2)     82 (21.5)     37 (18.0)     .31       Anemia     25 (4.3)     18 (4.7)     7 (3.4)     .45       Maligia     179 (30.4)     111 (29.1)     66 (32)     .46       Outcome measures no. (%)      24	COPD	47 (8.0)	27 (7.1)	20 (9.7)	.18
ESRD     77 (13.1)     53 (13.9)     24 (11.7)     15       Astma     45 (7.7)     32 (8.4)     13 (6.3)     32       Malignant tumor     32 (5.4)     22 (5.8)     10 (4.9)     .44       Charlson's comorbidity index mean (SD)     2.0 (0.12)     2.0 (0.11)     2.0 (0.13)     .69       Symptoms/signs no. (%)         .69       Fever     505 (85.9)     318 (83.2)     187 (90.7)     <.01	chronic kidney disease	79 (13.4)	52 (13.6)	27 (13.1)	.57
Asthma $45(7.7)$ $32(8.4)$ $13(6.3)$ $.32$ Malignant tumor $32(5.4)$ $22(5.8)$ $10(4.9)$ $.44$ Charlson's comorbidity index mean (SD) $2.0(0.12)$ $2.0(0.11)$ $2.0(0.13)$ $.69$ Symptoms/signs no. (%) $*$ $*$ $*$ $*$ Fever $505(85.9)$ $318(83.2)$ $187(90.7)$ $< .01$ Cough $450(76.5)$ $303(79.3)$ $147(71.0)$ $.05$ Dyspnea $400(68.0)$ $264(69.1)$ $136(66.0)$ $.08$ Chest Pain $206(35.0)$ $141(36.9)$ $.65(31.6)$ $.19$ Respiratory illness $116(19.7)$ $76(19.9)$ $40(19.4)$ $.61$ Pneumonia $119(20.2)$ $82(21.5)$ $.37(18.0)$ $.31$ Anemia $25(4.3)$ $18(4.7)$ $.7(3.4)$ $.45$ Myalgia $179(30.4)$ $111(29.1)$ $.66(32)$ $.46$ Diarrhea $192(32.7)$ $124(32.5)$ $.68(33)$ $.66$ Outcome measures no. (%) $110(18.7)$ $.84(22.0)$ $.26(12.6)$ $.01^{**}$ Ventilator use $82(13.9)$ $.515(40.6)$ $.77(37.4)$ $.45$ Outcome measures mean (SD) $.79(9.1)$ $.89(9.3)$ $.88(8.6)$ $.98$ Hospital length of stay $.79(9.1)$ $.89(9.3)$ $.88(8.6)$ $.98$ Total (UD axy $.95(8.4)$ $.83(7.5)$ $.107(10.1)$ $.43$	ESRD	77 (13.1)	53 (13.9)	24(11.7)	.15
Malignant tumor   32 (5.4)   22 (5.8)   10 (4.9)   .44     Charlson's comorbidity index mean (SD)   2.0 (0.12)   2.0 (0.11)   2.0 (0.13)   .69     Symptoms/signs no. (%)   -   -   -   -   -   -   -   -   .69     Ever   505 (85.9)   318 (83.2)   187 (90.7)   <.01	Asthma	45 (7.7)	32 (8.4)	13 (6.3)	.32
Charlson's comorbidity index mean (SD) $2.0 (0.12)$ $2.0 (0.11)$ $2.0 (0.13)$ .69Symptoms/signs no. (%)Fever $505 (85.9)$ $Cough$ $450 (76.5)$ $303 (79.3)$ $147 (71.0)$ $0.5$ Dyspnea $400 (68.0)$ $264 (69.1)$ $136 (66.0)$ $0.69$ $Chest Pain$ $206 (35.0)$ $116 (19.7)$ $76 (19.9)$ $40 (19.4)$ .61Pneumonia $119 (20.2)$ $82 (21.5)$ $37 (18.0)$ $311$ Anemia $25 (4.3)$ $18 (4.7)$ $7 (3.4)$ $45$ Myalgia $179 (30.4)$ $111 (29.1)$ $66 (32)$ $0utcome measures no. (%)$ ICU Admission $110 (18.7)$ $84 (22.0)$ $26 (12.6)$ $20 (39.5)$ $155 (40.6)$ $77 (37.4)$ $45$ Outcome measures nean (SD)Hospital length of stay $7.9 (9.1)$ $8.9 (9.3)$ $8.8 (8.6)$ $9.5 (8.4)$ $8.3 (7.5)$ $107 (10.1)$ $43$	Malignant tumor	32 (5.4)	22 (5.8)	10 (4.9)	.44
Symptoms/signs no. (%)   505 (85.9)   318 (83.2)   187 (90.7)   <.01	Charlson's comorbidity index mean (SD)	2.0 (0.12)	2.0 (0.11)	2.0 (0.13)	.69
Fever505 (85.9) $318 (83.2)$ $187 (90.7)$ <.01Cough450 (76.5) $303 (79.3)$ $147 (71.0)$ .05Dyspnea400 (68.0) $264 (69.1)$ $136 (66.0)$ .08Chest Pain206 (35.0) $141 (36.9)$ .65 (31.6).19Respiratory illness116 (19.7)76 (19.9)40 (19.4).61Pneumonia119 (20.2)82 (21.5).37 (18.0).31Anemia25 (4.3)18 (4.7).7 (3.4).45Myalgia179 (30.4)111 (29.1).66 (32).46Diarrhea120 (32.7)124 (32.5).68 (33).66Outcome measures no. (%)IIIIII (18.7).84 (22.0).26 (12.6).<01***	Symptoms/signs no. (%)	. ,			
Cough $450(76.5)$ $303(79.3)$ $147(71.0)$ .05Dyspnea $400(68.0)$ $264(69.1)$ $136(66.0)$ .08Chest Pain $206(35.0)$ $141(36.9)$ $65(31.6)$ .19Respiratory illness $116(19.7)$ $76(19.9)$ $40(19.4)$ .61Pneumonia $119(20.2)$ $82(21.5)$ $37(18.0)$ .31Anemia $25(4.3)$ $18(4.7)$ $7(3.4)$ .45Myalgia $179(30.4)$ $111(29.1)$ $66(32)$ .46Diarrhea $192(32.7)$ $124(32.5)$ $68(33)$ .66Outcome measures no. (%)Ito (18.7) $84(22.0)$ $26(12.6)$ $<.01^{**}$ Ventilator use $82(13.9)$ $54(14.1)$ $28(13.6)$ .47Death $232(39.5)$ $155(40.6)$ $77(37.4)$ .45Outcome measures mean (SD)Ito (19.7) $8.9(9.3)$ $8.8(8.6)$ .98Total ICU Davs $9.5(8.4)$ $8.3(7.5)$ $10.7(10.1)$ .43	Fever	505 (85.9)	318 (83.2)	187 (90.7)	<.01
Dysprea400 (68.0) $264 (69.1)$ $136 (66.0)$ .08Chest Pain206 (35.0) $141 (36.9)$ $65 (31.6)$ .19Respiratory illness116 (19.7)76 (19.9) $40 (19.4)$ .61Pneumonia119 (20.2) $82 (21.5)$ $37 (18.0)$ .31Anemia25 (4.3)18 (4.7)7 (3.4).45Myalgia179 (30.4)111 (29.1)66 (32).46Diarrhea192 (32.7)124 (32.5)68 (33).66Outcome measures no. (%)III (18.7)84 (22.0)26 (12.6)<.01**	Cough	450 (76.5)	303 (79.3)	147 (71.0)	.05
Chest Pain $206(35.0)$ $141(36.9)$ $65(31.6)$ .19Respiratory illness $116(19.7)$ $76(19.9)$ $40(19.4)$ .61Pneumonia $119(20.2)$ $82(21.5)$ $37(18.0)$ .31Anemia $25(4.3)$ $18(4.7)$ $7(3.4)$ .45Myalgia $179(30.4)$ $111(29.1)$ .66(32).46Diarrhea $192(32.7)$ $124(32.5)$ .68(33).66Outcome measures no. (%)ICU Admission $110(18.7)$ $84(22.0)$ $26(12.6)$ $<.01^{**}$ Ventilator use $82(13.9)$ $54(14.1)$ $28(13.6)$ .47Death $232(39.5)$ $155(40.6)$ $77(37.4)$ .45Outcome measures mean (SD)Image: State Sta	Dyspnea	400 (68.0)	264 (69.1)	136 (66.0)	.08
Respiratory illness $116(19.7)$ $76(19.9)$ $40(19.4)$ .61Pneumonia $119(20.2)$ $82(21.5)$ $37(18.0)$ .31Anemia $25(4.3)$ $18(4.7)$ $7(3.4)$ .45Myalgia $179(30.4)$ $111(29.1)$ $66(32)$ .46Diarrhea $192(32.7)$ $124(32.5)$ $68(33)$ .66Outcome measures no. (%)ICU Admission $110(18.7)$ $84(22.0)$ $26(12.6)$ $<.01^{**}$ Ventilator use $82(13.9)$ $54(14.1)$ $28(13.6)$ .47Death $232(39.5)$ $155(40.6)$ $77(37.4)$ .45Outcome measures mean (SD)Image: State of the state of th	Chest Pain	206 (35.0)	141 (36.9)	65 (31.6)	.19
Pneumonia $119(20.2)$ $82(21.5)$ $37(18.0)$ $.31$ Anemia $25(4.3)$ $18(4.7)$ $7(3.4)$ $.45$ Myalgia $179(30.4)$ $111(29.1)$ $66(32)$ $.46$ Diarrhea $192(32.7)$ $124(32.5)$ $68(33)$ $.66$ Outcome measures no.(%)III.0 (18.7) $84(22.0)$ $26(12.6)$ $<01^{**}$ Ventilator use $82(13.9)$ $54(14.1)$ $28(13.6)$ $.47$ Death $232(39.5)$ $155(40.6)$ $.77(37.4)$ $.45$ Outcome measures mean (SD)Image: State of the state of th	Respiratory illness	116 (19.7)	76 (19.9)	40 (19.4)	.61
Anemia $25$ (4.3) $18$ (4.7) $7$ (3.4) $45$ Myalgia $179$ (30.4) $111$ (29.1) $66$ (32).46Diarrhea $192$ (32.7) $124$ (32.5) $68$ (33).66Outcome measures no. (%) $I10$ (18.7) $84$ (22.0) $26$ (12.6) $<01^{**}$ Ventilator use $82$ (13.9) $54$ (14.1) $28$ (13.6).47Death $232$ (39.5) $155$ (40.6) $77$ (37.4).45Outcome measures mean (SD) $I10$ (18.7) $8.9$ (9.3) $8.8$ (8.6).98Total ICU Davs $9.5$ (8.4) $8.3$ (7.5) $10.7$ (10.1).43	Pneumonia	119 (20.2)	82 (21.5)	37 (18.0)	.31
Myalgia     179 (30.4)     111 (29.1)     66 (32)     .46       Diarrhea     192 (32.7)     124 (32.5)     68 (33)     .66       Outcome measures no. (%)     III (18.7)     84 (22.0)     26 (12.6)     <.01**	Anemia	25 (4.3)	18 (4.7)	7 (3.4)	.45
Diarrhea     192 (32.7)     124 (32.5)     68 (33)     .66       Outcome measures no. (%)     ICU Admission     110 (18.7)     84 (22.0)     26 (12.6)     <.01**	Myalgia	179 (30.4)	111 (29.1)	66 (32)	.46
Outcome measures no. (%)     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X     X <thx< th="">     X     X     X</thx<>	Diarrhea	192 (32.7)	124 (32.5)	68 (33)	.66
ICU Admission     110 (18.7)     84 (22.0)     26 (12.6)     <.01**       Ventilator use     82 (13.9)     54 (14.1)     28 (13.6)     .47       Death     232 (39.5)     155 (40.6)     77 (37.4)     .45       Outcome measures mean (SD)     Hospital length of stay     7.9 (9.1)     8.9 (9.3)     8.8 (8.6)     .98       Total ICU Davs     9.5 (8.4)     8.3 (7.5)     10.7 (10.1)     .43	Outcome measures no. (%)				
Ventilator use     82 (13.9)     54 (14.1)     28 (13.6)     .47       Death     23 (39.5)     155 (40.6)     77 (37.4)     .45       Outcome measures mean (SD)     Hospital length of stay     7.9 (9.1)     8.9 (9.3)     8.8 (8.6)     .98       Total ICU Days     9.5 (8.4)     8.3 (7.5)     10.7 (10.1)     .43	ICU Admission	110(18.7)	84 (22.0)	26(12.6)	<.01**
Death     232 (39.5)     155 (40.6)     77 (37.4)     .45       Outcome measures mean (SD)	Ventilator use	82 (13.9)	54 (14.1)	28 (13.6)	.47
Outcome measures mean (SD) 1000000000000000000000000000000000000	Death	232 (39.5)	155 (40.6)	77 (37.4)	.45
Hospital length of stay     7.9 (9.1)     8.9 (9.3)     8.8 (8.6)     .98       Total ICU Days     9.5 (8.4)     8.3 (7.5)     10.7 (10.1)     43	Outcome measures mean (SD)	()	( )		
Total ICU Davs 95 (8.4) 8.3 (7.5) 10.7 (10.1) 43	Hospital length of stav	7.9 (9.1)	8.9 (9.3)	8.8 (8.6)	.98
	Total ICU Davs	9.5 (8.4)	8.3 (7.5)	10.7 (10.1)	.43

Abbreviations: BMI, body mass index; COVID-19, corona virus disease 2019; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; ESRD, end stage renal disease; ICU, intensive care unit; RCT-PCR, reverse transcription-polymerase chain reaction; mean (SD), mean (standard deviation); no. (%), number (percent); SUNY, State University New York.

\**P*-value significant at ≤.05;

\*\**P*-value significant at  $\leq$ .0125 level controlling for family wise error.

disease; and included length of hospital stay (when not used as the outcome); demographic variables, co-morbid conditions and presenting symptoms/signs (Table 2). Statistical analyses were performed using SAS Institute Inc. version 9.4.

# RESULTS

Tables 1 shows the demographic and clinical characteristics of the 588 COVID-19 hospitalized patients. Of the 588 reverse transcription-polymerase chain reaction (RCT-PCR) confirmed COVID-19 positives, 35% self-reported being flu-vaccinated, 47.1% were women, 88.3% were black, 18.7% required ICU-admission, 13.9% required ventilator-use, and 39.5% died during in-hospital stay. The mean (SD) age was 68.4 (14.5) years, BMI was 30.3 (9.5) kg/m<sup>2</sup>, and length of stay was 7.9 (9.1) days. Hypertension (79.4%), diabetes (52.9%) and hyperlipidemia (34.9%) were also the most common comorbidities. Fever (85.9%), cough (76.5%), and dyspnea (68.0%) were the three most common COVID-19 symptoms. Rates for both self-reported flu-vaccinated statuses (No vs Yes) did not significantly differ for ventilatoruse {[54/382] vs [28/206], *P* = .47 and mortality {[155/382] vs [77/ 206], P = .45] respectively. Mean [SD] for both hospital length of stay and total ICU days did not significantly differ for self-reported fluvaccinated statuses (No vs Yes) {8.9 [9.3] vs 8.8 [8.6], P = .98 and {8.3 [7.5] vs 10.7 [10.1], P = .43, respectively}. Bivariate analysis showed that ICU admission rates differed significantly between self-reported

flu-vaccinated statuses (No vs Yes) {[84/382] vs [26/206], OR: 1.95, 95%CI: 1.21-3.15, P <.001}, with adjusted analyses showing a significantly increased likelihood of ICU-admission among self-reported nonflu-vaccinated relative to self-reported flu-vaccinated patients (aOR: 1.88, 95%CI: 1.18-3.99, P < .01). Furthermore, stratified adjusted analyses by age and BMI respectively showed a significantly increased likelihood of requiring an ICU admission among self-reported non-flu-vaccinated relative to self-reported flu-vaccinated patients only for ages <65 (aOR: 4.16, 95%CI: 1.03-16.73), and nonobese patients (aOR: 2.61, 95%CI: 1.35-5.03) (Table 2).

# DISCUSSION

In this sample of COVID-19 hospitalized patients in Brooklyn, during the first wave of the COVID-19 pandemic, mortality and ventilation rates were actually higher in non-flu-vaccinated patients compared to flu-vaccinated patients but the differences were not statistically significant. However, non-flu-vaccinated hospitalized patients were two times more likely to have required an ICU admission, relative to flu-vaccinated hospitalized patients after adjusting for pertinent confounders. Stratified analysis of this association showed effects significantly stronger and present for ages <65 and non-obese patients. Non-flu-vaccinated patients aged <65 and nonobese patients were four and approximately three times more likely to have required an ICU admission, relative to their flu-vaccinated

#### Table 2

Adjusted Odds Ratios for the association between Self-reported Flu vaccination (No vs Yes) and categorical outcome measures {RCT-PCR COVID-19 POSITIVES}

Outcome Variable	Crude Odds Ratios (95% CI)	P-value	‡Adjusted Odds Ratios (95% CI)	P-value			
ICU Admission	1.95 (1.21-3.15)	<.01**	1.88 (1.18-3.99)	<.01**			
Ventilator use	1.05 (0.64-1.71)	.85	0.94 (0.43-2.06)	.88			
Death	1.14 (0.81-1.62)	.45	0.87 (0.47-1.62)	.67			
Adjusted risk ratios for the association between self-reported flu vaccination (No vs Yes) and continuous outcome measures (RCT-PCR COVID-19 POSITIVES)							
Hospital length of stay	1.07 (0.42-1.72)	.81	0.84 (0.33-1.94)	.87			
Total ICU Days	0.94 (0.36-2.52)	.79	0.72 (0.37-2.07)	.84			
Adjusted odds ratios for the association between Self-reported Flu vaccination (No vs Yes) and categorical outcome measures stratified by Age and BMI							
RCT-PCR COVID-19 Positives {Ages <65 only}							
ICU admission	2.81 (1.23-6.45)	.01**	4.16 (1.03-16.73)	.04*			
Ventilator use	1.46 (0.61-3.48)	.39	1.89 (0.53-6.77)	.33			
Death	1.62 (0.78-3.37)	.20	0.80 (0.24-2.64)	.72			
RCT-PCR COVID-19 Positives {Ages $\geq$ 65 only}							
ICU admission	1.57 (0.87-2.83)	.1321	2.03 (0.66-6.27)	.22			
Ventilator use	0.88 (0.43-1.61)	.68	0.57 (0.20-1.61)	.29			
Death	1.07 (0.70-1.62)	.76	1.03 (0.48-2.21)	.95			
RCT-PCR COVID-19 Positives {BMI <30 only}							
ICU admission	2.32 (1.31-4.11)	<.01**	2.61 (1.35-5.03)	<.01**			
Ventilator use	1.17 (0.66-2.06)	.61	1.21 (0.63-2.30)	.57			
Death	1.23 (0.84-1.80)	.29	1.23 (0.79-1.91)	.35			
RCT-PCR COVID-19 Positives {BMI ≥30 only}							
ICU admission	1.24 (0.49 - 3.12)	.65	1.12 (0.38-3.31)	.84			
Ventilator use	0.74 (0.27 - 2.01)	.55	0.80 (0.27-2.39)	.69			
Death	0.79 (0.33 - 1.86)	.58	0.71 (0.23-2.18)	.55			
Adjusted risk ratios for the association between self-reported flu vaccination (No vs Yes) and continuous outcome measures stratified by age and BMI							
RCT-PCR COVID-19 Positives (Ages <65 only)							
Hospital length of stay	1.12 (0.47-2.77)	.76	1.00 (0.45-2.57)	.57			
Total ICU Days	0.89 (0.41-3.37)	.84	1.01 (0.38-3.63)	.73			
RCT-PCR COVID-19 Positives {Ages ≥65 only}							
Hospital length of stay	0.92 (0.34-2.51)	.86	0.89 (0.46-2.32)	.77			
Total ICU Days	1.09 (0.41-2.77)	.64	1.02 (0.58-2.46)	.83			
RCT-PCR COVID-19 Positives {BMI <30 only}							
Hospital length of stay	1.11 (0.58-2.64)	.41	1.03 (0.43-2.62)	.61			
Total ICU Days	1.33 (0.76-3.91)	.49	1.23 (0.69-3.82)	.37			
RCT-PCR COVID-19 Positives (BMI ≥30 only)							
Ventilator use	0.86 (0.39-2.33)	.55	1.01 (0.37-2.65)	.58			
Death	0.93 (0.47-4.39)	.48	0.81 (0.33-4.28)	.45			

*Abbreviations*: BMI, body mass index; COVID-19, corona virus disease 2019; ICU, intensive care unit; RCT-PCR, reverse transcription-polymerase chain reaction. \**P*-value significant at <.05;

\*\**P*-value significant at  $\leq$ .0125 level;

<sup>‡</sup>Adjusted for the following covariates/potential confounders selected *a priori:* length of hospital stay; age, sex, race and body mass index (BMI); hypertension, diabetes, coronary artery disease, stroke, chronic kidney disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), end stage renal disease (ESRD), asthma, malignant tumor; fever, cough, dyspnea, chest pain, respiratory illness, pneumonia, anemia, myalgia, and diarrhea. Statistical analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, North Carolina, USA).

hospitalized counterparts, respectively. Our findings suggest that the risk of non-obese and ages <65 patients requiring an ICU-admission due to COVID-19 may be reduced if they were flu-vaccinated. A recent study found that higher regional rates of flu-vaccinated adults >65 years old was associated with lower regional rates of COVID-19 deaths.<sup>6</sup> We did not find any association between flu-vaccination and hospital length of stay, total ICU days, mechanical ventilator use, and mortality perhaps due to the low prevalence of flu vaccination in this Brooklyn patient sample and in the US overall (36% vs 48%).<sup>7</sup> Possible explanations of this finding could be the well-documented protective effects of flu-vaccination for co-morbid conditions.<sup>8-10</sup> Flu vaccine behavior is a marker for patients' healthy behaviors and this could possibly explain the findings. It also could be because of an already primed innate immunity from flu-vaccination, especially in <65 year old and non-obese, that results in an effective rapid immunogenic response.<sup>11</sup> However, it seems that once a certain threshold is reached, possibly due to an overwhelming and immunosuppressive inflammatory/cytokine storm,<sup>12</sup> that necessitates an ICU-admission, the protective effect is no longer seen. Importantly, these findings add significant rationale supporting the public health promotion of flu-vaccination suggesting that this could mitigate the enormous demand for critical care that can overwhelm healthcare systems especially with possible escalating COVID-19 infections during the flu season and second wave.

#### Limitation

The key limitation of this study is the self-report assessment of fluvaccination. Future studies should use objective measures of flu-vaccination and evaluate possible mechanisms explaining this association.

# CONCLUSIONS

Our findings suggest that public health promotion of flu-vaccination may help mitigate the overwhelming demand for critical COVID-19 care that devastated underserved communities and under sourced healthcare systems, especially as we patiently wait for the large-scale availability of COVID-19 vaccines.

#### Data sharing

Deidentified patient data collected for the study, the statistical analysis plan and a data dictionary defining each field in the set, will be made available upon request. Data will be shared with investigator support after approval of the IRB and a signed data access agreement.

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