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Real world SARS-COV-2 vaccine effectiveness in a Miami academic institution

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Abstract

Background: To assess the effectiveness of messenger RNA vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) in preventing emergency department (ED) presentations for acute respiratory illness.

Basic procedures: We conducted a retrospective study assessing adult presentations (age ≥18) to the University of Miami Hospital’s ED from January 1st through August 25th, 2021, with a SARS-COV-2 PCR test and acute respiratory infection symptoms. Vaccine effectiveness was calculated using a test-negative design. Both univariable and multivariable (adjusted for age, gender, race, insurance status, imputed body mass index [BMI], vaccine type, week of presentation) regression analyses were conducted for the full cohort and subgroups.

Main findings: The cohort consisted of 13,203 ED presentations—3134 (23.7%) fully vaccinated and SARS-COV-2 negative, 108 (0.8%) fully vaccinated and SARS-COV-2 positive, 8817 (66.8%) unvaccinated and SARS-COV-2 negative, and 1144 (8.7%) unvaccinated and SARS-COV-2 positive. Unadjusted vaccination effectiveness was 73.4% (95% confidence interval: 67.5%, 78.3%) and, after adjustment, 73.8% (66.2%, 79.7%). The Moderna vaccine’s effectiveness was numerically higher (unadjusted: 78.2% [68.8%, 84.7%]; adjusted: 78.0% [68.1%, 84.9%]) than the Pfizer vaccine’s (unadjusted: 70.8% [62.9%, 76.9%]; adjusted: 73.9% [66.3%, 79.8%]). We found a significant difference in adjusted vaccine effectiveness across categories was BMI (p < 0.001)—BMI <25: 66.3% (45.3%, 79.2%); BMI 25–29: 71.3% (56.1%, 81.2%); BMI 30–34: 84.5% (71.7%, 91.5%); and BMI ≥35: 72.7% (50.5%, 84.9%).

Principal conclusions: We demonstrated excellent real-world effectiveness of mRNA vaccines in preventing ED presentation for SARS-COV-2 in a diverse U.S. cohort. Notably, vaccine effectiveness improved with increasing BMI (until class 2 obesity).

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1. Introduction

Two messenger RNA vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) were released to the general population at the turn of 2020. These vaccines were shown to be 94.1 and 95% efficacious at preventing symptomatic SARS-COV-2 infection [1,2]. While numerous trials have evaluated the effectiveness of severe SARS-COV-2 vaccinations in healthcare workers [3-5] and inpatients [6,7], there remains a paucity of data in the general U.S. population presenting to the Emergency Department (ED). Moreover, focus has been primarily on the prevention of severe disease; less is known about significant disease which may not require hospitalization. In this study, we assessed vaccine effectiveness in preventing ED presentations for acute respiratory illness.

2. Methods

We conducted a retrospective study assessing adult presentations (age ≥18) to the University of Miami Hospital’s ED from January 1st through August 25th, 2021, with a SARS-COV-2 PCR test and acute respiratory infection symptoms, identified using ICD-10 codes. Institutional review board approval was obtained from the University of Miami (20200739). Presentations were classified into three groups: (1) Fully vaccinated: 14 days after 2nd mRNA vaccine dose; (2) Partially
vaccinated: received at least one dose but not fully vaccinated; (3) Unvaccinated. Single dose adenovirus vaccination was excluded from our analysis due to the low frequency of receipt in our population. Vaccination status was obtained at the time of ED presentation through the electronic medical record (EMR) which is synced with the state registry, Florida Shots. Manual extraction of vaccination data from Florida Shots for 50 randomly selected presentations (25 fully vaccinated, 25 unvaccinated in the EMR) was performed to assess EMR accuracy.

Vaccine effectiveness was calculated using a test-negative design, previously described [6,8] (Fig. 1). Primary analyses compared fully vaccinated to unvaccinated presentations (partially vaccinated presentations excluded); we performed a sensitivity analysis including presentations with partial vaccination as a separate exposure group. Both univariable and multivariable (adjusted for age, gender, race, insurance status, imputed body mass index [BMI], vaccine type) regression analyses were conducted for the full cohort and subgroups (with assessment of subgroup-related differences by inclusion of interaction terms in full cohort model). Because of the temporal variability in SARS-COV-2 case positivity and vaccination rates, we also adjusted for week of ED visit (as restricted cubic splines with 4 knots). All statistics were performed in STATA 16 (College Station, TX).

3. Results

The cohort consisted of 13,203 ED presentations—3134 (23.7%) fully vaccinated and SARS-COV-2 negative, 108 (0.8%) fully vaccinated and SARS-COV-2 positive, 8817 (66.8%) unvaccinated and SARS-COV-2 negative, and 1144 (8.7%) unvaccinated and SARS-COV-2 positive. Unvaccinated patients tended to be younger and more commonly insured by Medicaid (Table 1). Random sampling manual review, via our state database, demonstrated perfect positive and negative predictive value (100%) of true vaccination status by EMR documentation.

Unadjusted full vaccination effectiveness was 73.4% (95% CI 67.5%, 78.3%) and, after adjustment, 73.8% (66.2%, 79.7%). The Moderna vaccine’s effectiveness was numerically higher (unadjusted: 78.2% [68.8%, 84.7%]; adjusted: 78.0% [68.1%, 84.9%]) than the Pfizer vaccine’s (unadjusted: 70.8% [62.9%, 76.9%]; adjusted: 73.9% [66.3%, 79.8%]; Fig. 2). While differences were noted in the unadjusted vaccine effectiveness by age, race, payor, and BMI (p < 0.001), the only subgroups with a significant difference in adjusted vaccine effectiveness was BMI (p < 0.001)—BMI <25: 66.3% (45.3%, 79.2%); BMI 25–29: 71.3% (56.1%, 81.2%); BMI 30–34: 84.5% (71.7%, 91.5%); and BMI ≥35: 72.7% (50.5%, 84.9%).

Sensitivity analysis was performed with 14,173 presentations, 970 of which were partially vaccinated. The effectiveness of partial vaccination was 36.3% (18.7%, 50.2%) unadjusted and 19.6% (−4.7%, 38.2%) adjusted; in this cohort, the adjusted effectiveness of full vaccination was 64.0% (55.1%, 71.2%).

4. Discussion

In this study, we demonstrate excellent real-world effectiveness of mRNA vaccines in preventing ED presentation for SARS-COV-2 in a diverse U.S. cohort. Notably, vaccine effectiveness improved with increasing BMI (until class 2 obesity), with the highest effectiveness among those with a BMI of 30–34. There was no statistically significant difference in adjusted vaccine effectiveness among patients of different genders, ages, races, ethnicities or payors.

To our knowledge, this is the first study to evaluate vaccine effectiveness in preventing, specifically, ED presentations. A recent publication demonstrated a higher mRNA vaccine effectiveness (91% vs our 73.8%) at preventing ED or urgent care visits [6]. Three major differences exist between this study and ours. First, Thompson et al. [6] included urgent care visits; however, this inclusion of a presumably less acutely ill population would be likely bias towards a reduced vaccine effectiveness. A second important difference was the time period of study, notably our inclusion of presentations during the summer of 2021. During this time the delta variant became predominant in the U.S. [9], and vaccines have been found to be less effective in preventing delta-related symptomatic SARS-COV-2 infection [10]. Notably, we test and genotype all our ED presentations with acute upper respiratory symptoms, and the delta variant accounted for nearly 100% of the SARS-COV-2 infections as of July 2021. Finally, the two cohorts studied differed substantially—ours was younger (58.8% vs 34% <65 years-old) and more racially/ethnically diverse (69.3% vs 82% White and 42.6% vs 84% non-Hispanic). While adjustments for these measured differences were made, it is unclear whether and to what extent coincident unmeasured differences may have contributed to our disparate results.

Our study is novel in focusing on ED presentations for SARS-CoV-2, a more expansive marker of significant disease than hospitalization alone, in a diverse U.S. cohort. There are, however, limitations. First, we only had 108 cases of vaccinated SARS-COV-2 and <10 in some subgroups; even a single additional case would meaningfully impact our calculations for these. Second, we did not verify all presentations’ vaccination status through registries. Our manual review suggests that vaccination misclassification is rare to non-existent, though. Third, our cohort included more vaccinations with Pfizer than Moderna; whether this disproportionality impacted our results is unknown. Last, as our study is retrospective in nature, the impact of residual confounding despite multivariable adjustment cannot be fully excluded.
### Table 1
Cohort characteristics.

| Characteristic | Overall a | Fully vaccinated & COVID- | Fully vaccinated & COVID+ | Not vaccinated & COVID- | Not vaccinated & COVID+ |
|----------------|-----------|---------------------------|--------------------------|------------------------|------------------------|
| # of ED Presentations, # (row %) | 13,203 (100%) | 3134 (23.7%) | 108 (0.8%) | 8817 (66.8%) | 1144 (8.7%) |
| Vaccination typeb | | | | | |
| mRNA, Moderna | 1162 (8.8%) | 1130 (36.0%) | 32 (29.6%) | n/a | n/a |
| mRNA, Pfizer | 2080 (15.8%) | 2004 (63.9%) | 76 (70.4%) | n/a | n/a |
| Age (years), median (IQR) | | | | | |
| Male Sex | 707 (5.4%) | 159 (5.1%) | 5 (4.6%) | 4831 (54.8%) | 649 (56.7%) |
| Race | | | | | |
| White | 9,147 (69.3%) | 2525 (80.6%) | 86 (79.6%) | 5865 (66.5%) | 671 (58.7%) |
| Black | 3349 (25.4%) | 450 (14.4%) | 17 (15.7%) | 2484 (28.2%) | 398 (34.8%) |
| Other/Unknown | 707 (5.4%) | 159 (5.1%) | 5 (4.6%) | 468 (5.3%) | 75 (6.6%) |
| Ethnicity | | | | | |
| Non-Hispanic | 5621 (42.6%) | 1311 (41.8%) | 40 (37.0%) | 3795 (43.0%) | 475 (41.5%) |
| Hispanic | 7312 (55.4%) | 1766 (56.3%) | 66 (61.1%) | 4831 (54.8%) | 649 (56.7%) |
| Other/Unknown | 270 (2%) | 57 (1.8%) | 2 (1.9%) | 191 (2.2%) | 20 (1.7%) |
| Elixhauser Comorbiditiesd | | | | | |
| Congestive heart failure | 2391 (18.1%) | 604 (19.2%) | 14 (13.0%) | 1674 (19.0%) | 99 (8.7%) |
| Valvular disease | 2446 (18.5%) | 729 (23.3%) | 22 (20.4%) | 1606 (18.2%) | 89 (7.8%) |
| Peripheral vascular disorders | 2397 (18.2%) | 696 (22.2%) | 7 (6.5%) | 1608 (18.2%) | 89 (7.8%) |
| Hypertension | 8799 (66.6%) | 2351 (75.0%) | 70 (64.8%) | 5779 (65.5%) | 599 (52.4%) |
| Neurologic disorders | 3010 (22.8%) | 776 (24.8%) | 15 (13.9%) | 2104 (23.9%) | 115 (10.1%) |
| Chronic pulmonary disease | | | | | |
| Diabetes mellitus | | | | | |
| Uncomplicated | 3780 (28.6%) | 975 (31.1%) | 40 (37.0%) | 2485 (28.2%) | 280 (18.2%) |
| Complicated | 3450 (26.1%) | 882 (28.1%) | 29 (26.9%) | 2310 (26.2%) | 229 (20.0%) |
| Hypothyroidism | 1936 (14.7%) | 587 (18.7%) | 15 (13.9%) | 1245 (14.1%) | 89 (7.8%) |
| Renal Failure | 2591 (19.6%) | 692 (22.1%) | 27 (25.0%) | 1745 (19.8%) | 127 (11.1%) |
| Liver failure | 2179 (16.5%) | 583 (18.6%) | 9 (8.3%) | 1672 (19.0%) | 99 (8.7%) |
| Metastatic cancer | 2380 (18.0%) | 649 (20.7%) | 7 (6.5%) | 1672 (19.0%) | 99 (8.7%) |
| Solid tumor (no metastases) | 3520 (26.7%) | 940 (30.0%) | 20 (18.5%) | 2351 (26.7%) | 209 (18.3%) |
| Coagulopathy | 2361 (17.9%) | 567 (18.1%) | 12 (11.1%) | 1671 (19.0%) | 111 (9.7%) |
| Obesity | 4465 (33.8%) | 1131 (36.1%) | 34 (31.5%) | 2959 (33.6%) | 341 (29.8%) |
| Weight loss | 2657 (20.1%) | 642 (20.5%) | 12 (11.1%) | 1926 (21.8%) | 77 (6.7%) |
| Fluid & electrolyte disorders | 6401 (48.5%) | 1480 (47.2%) | 36 (33.3%) | 4485 (50.9%) | 400 (35.0%) |
| Deficiency anemia | 2966 (22.5%) | 753 (24.0%) | 18 (16.7%) | 2092 (23.7%) | 103 (9.0%) |
| Depression | 2966 (22.5%) | 753 (24.0%) | 18 (16.7%) | 2092 (23.7%) | 103 (9.0%) |
| Body mass indexe | | | | | |
| <25 | 4803 (36.4%) | 1112 (35.5%) | 27 (25.0%) | 3406 (38.6%) | 258 (22.6%) |
| 25–30 | 4074 (31.9%) | 1024 (32.7%) | 37 (34.3%) | 2676 (30.4%) | 337 (29.5%) |
| 30–35 | 2292 (17.4%) | 567 (18.1%) | 20 (18.5%) | 1432 (16.2%) | 273 (23.9%) |
| >35 | 1871 (14.2%) | 419 (13.4%) | 21 (19.4%) | 1199 (13.6%) | 232 (20.3%) |
| Insurance | | | | | |
| Commercial | 4597 (34.8%) | 1036 (33.1%) | 33 (30.6%) | 3107 (35.2%) | 421 (36.8%) |
| Medicaid | 1880 (14.2%) | 243 (7.8%) | 5 (4.6%) | 1482 (16.8%) | 150 (13.1%) |
| Medicare | 5594 (42.4%) | 1761 (56.2%) | 55 (50.0%) | 3434 (38.9%) | 344 (30.1%) |
| Other | 1132 (8.6%) | 94 (3.0%) | 15 (13.9%) | 794 (9.0%) | 229 (20%) |
| Maximum SOFA score within 24 h of ED presentationf, median (IQR) | 1 (0.2) | 1 (0.2) | 1 (0.3) | 1 (0.2) | 1 (0.2) |
| Outcomes | | | | | |
| Admitted to hospital from ED | 9894 (75%) | 2598 (26.0%) | 41 (38.0%) | 6768 (76.8%) | 516 (45.1%) |
| Final ED or hospital dispositiong | | | | | |
| Death | 614 (4.7%) | 120 (4.8%) | 5 (4.6%) | 431 (4.9%) | 58 (5.1%) |
| Facility | 896 (6.8%) | 225 (7.2%) | 4 (3.7%) | 601 (6.8%) | 66 (5.8%) |
| Home | 11,671 (88.4%) | 2786 (88.9%) | 99 (91.7%) | 7771 (88.1%) | 1015 (88.7%) |

ED: emergency department; IQR: interquartile range; SOFA: sequential organ failure assessment.

* Inclusive of fully vaccinated and unvaccinated.

b No vaccinations with adenovirus-based vaccines were included in the cohort.

c 1 (0.008%) missing data on age.

Elixhauser Comorbidities were < 10% of the full cohort and included: pulmonary circulation disorders, 5.3%; paralysis, 5.7%; peptic ulcer disease, 5.2%; AIDS, 2.0%; lymphoma, 6.0%; rheumatoid arthritis/collagen vascular disease, 5.9%; blood loss anemia, 6.3%; alcohol abuse, 4.6%; drug abuse, 6.0%; and psychoses, 6.3%.

e 163 (1.23%) missing data on body mass index.

f 259 (1.96%) missing data on SOFA score.

g 22 (0.17%) remained as hospital admissions at the time of data collection.

h All five vaccinated patients who died were in high risk categories: three were ≥ 85 years old; one was 65 years old with pulmonary fibrosis on mycophenolate; and, one was 74 years old with pulmonary fibrosis.
Fig. 2. Forest Plots demonstrating Vaccine Effectiveness. Panel A displays the unadjusted vaccine effectiveness. Panel B shows the adjusted vaccine effectiveness.
This study demonstrates excellent real-world effectiveness of SARS-COV-2 mRNA vaccines in preventing significant disease in a diverse U.S. population.

Presentations
None.

Author contributions
CM, TF, BS, PW, MS, DP and HG all contributed to the study design. CM contributed to the analysis and interpretation of the data, drafting of the manuscript, and critical revision of the manuscript. HG contributed to the analysis and interpretation of the data, and critical revision of the manuscript. PW contributed to data acquisition, analysis of the data and revision of the manuscript. TF, BS, MS, and DP contributed to the interpretation of the data and revision of the manuscript.

Disclosures
Mr. Warde and Dr.'s Shukla, Sosa, and Gershengorn received funding from University of Miami Hospital and Clinics data analytics research team.

CRediT authorship contribution statement
Christopher Mallow: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. Tanira Ferreira: Writing – review & editing, Methodology, Investigation, Conceptualization. Bhavarth Shukla: Writing – review & editing, Methodology, Investigation, Conceptualization. Prem Warde: Writing – review & editing, Formal analysis, Data curation, Conceptualization. Marie Anne Sosa: Writing – review & editing, Methodology, Investigation, Conceptualization. Dipen J. Parekh: Writing – review & editing, Methodology, Investigation, Conceptualization. Hayley B. Gershengorn: Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest
Dr’s Shukla, Sosa, and Gershengorn received funding from University of Miami Hospital and Clinics data analytics research team.

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