Effectiveness of the Ad26.COV2.S (Johnson & Johnson) COVID-19 Vaccine for Preventing COVID-19 Hospitalizations and Progression to High Disease Severity in the United States

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Running Title

Effectiveness of the Ad26.COV2.S COVID-19 Vaccine

Abstract

Background

Adults in the United States (US) began receiving the viral vector COVID-19 vaccine, Ad26.COV2.S (Johnson & Johnson [Janssen]), in February 2021. We evaluated Ad26.COV2.S vaccine effectiveness (VE) against COVID-19 hospitalization and high disease severity during the first 10 months of its use.

Methods

In a multicenter case-control analysis of US adults (≥18 years) hospitalized March 11–December 15, 2021, we estimated VE against susceptibility to COVID-19 hospitalization (VEs), comparing odds of prior vaccination with a single dose Ad26.COV2.S vaccine between hospitalized cases with COVID-19 and controls without COVID-19. Among hospitalized patients with COVID-19, we estimated VE against disease progression (VEp) to death or invasive mechanical ventilation (IMV), comparing odds of prior vaccination between patients with and without progression.

Results

After excluding patients receiving mRNA vaccines, among 3,979 COVID-19 case-patients (5% vaccinated with Ad26.COV2.S) and 2.229 controls (13% vaccinated with Ad26.COV2.S), VEs of Ad26.COV2.S against COVID-19 hospitalization was 70% (95% CI: 63%–75%) overall, including 55% (29%–72%) among immunocompromised patients, and 72% (64%–77%) among immunocompetent patients, for whom VEs was similar at 14–90 days (73% [59%–82%]), 91–180 days (71% [60%–80%]), and 181–274 days (70% [54%–81%]) post-vaccination. Among hospitalized COVID-19 case-patients, VEp was 46% (18%–65%) among immunocompetent patients.

Conclusions

The Ad26.COV2.S COVID-19 vaccine reduced the risk of COVID-19 hospitalization by 72% among immunocompetent adults without waning through 6 months post-vaccination. After hospitalization for COVID-19, vaccinated immunocompetent patients were less likely to require IMV or die compared to unvaccinated immunocompetent patients.

Key words: COVID-19, vaccine effectiveness, viral vector vaccines

Background

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), resulted in more than 7 million hospitalizations and 890,000 deaths in the United States (US) through January 2022[1]. In February 2021, the SARS-CoV-2 viral vector vaccine (Ad26.COV2.S) from Johnson & Johnson (Janssen), became the third of three vaccines (in addition to BNT162b2 from Pfizer-BioNTech and mRNA-1273 from Moderna in December 2020) to be made available in the United States (US) for adults aged ≥18 years under Emergency Use Authorization by the Food and Drug Administration (FDA).[2] This vaccine employs a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector encoding a full-length SARS-CoV-2 spike protein[3] and has been shown in clinical trials[4,5] and early observational studies[6,7] to be effective in preventing severe COVID-19.

Most people vaccinated against COVID-19 in the US have received one of the two mRNA COVID-19 vaccines (BNT162b2 or mRNA-1273). However, approximately 18 million doses of the Ad26.COV2.S vaccine have been administered in the US through February 2022.[1] Less frequent use of the Ad26.COV2.S vaccine may be due to later authorization than mRNA vaccines, limited availability in many locations, lower estimated vaccine effectiveness (VE) compared with mRNA vaccines,[6] or early reports of adverse events including thrombosis with thrombocytopenia syndrome (TTS),[8,9] leading to a temporary suspension of use from April 13–23, 2021, followed by resumed use with a warning about the risk of rare blood clotting events.[9] In December 2021, the United States Centers for Disease Control and Prevention (CDC) issued a preferential recommendation for the BNT162b2 and mRNA-1273 mRNA vaccines over the Ad26.COV2.S vaccine for primary and booster vaccination.[10]

Due to its comparatively limited use, real-world evaluations of VE for the Ad26.COV2.S vaccine against COVID-19 hospitalization[6] have been relatively limited compared to those for mRNA vaccines.[11–14] However, in the US, the Ad26.COV2.S vaccine continues to have a role in preventing COVID-19, including for persons with a contraindication to receipt of mRNA COVID-19 vaccines.[9] In addition, Johnson and

Johnson plans to donate almost 100 million doses of Ad26.COV2.S internationally through the COVAX program led by the Coalition for Epidemic Preparedness Innovations, Gavi Vaccine Alliance, and the World Health Organization.[15] Therefore, evaluations to assess the real-world effectiveness of the Ad26.COV2.S vaccine against severe COVID-19 are important. Ongoing use of the Ad26.COV2.S vaccine in the US population since February 2021 means that evaluations of VE against hospitalization with sufficient sample size to be meaningful are now possible. In this analysis, we evaluated two forms of vaccine effectiveness[16] of the Ad26.COV2.S vaccine: (1) effectiveness in preventing susceptibility to COVID-19-associated hospitalization (VEs), and (2) effectiveness against the progression of COVID-19 to death or invasive mechanical ventilation (IMV) within 28 days of hospitalization (VEp) as a measure of potential disease attenuation among vaccinated patients with COVID-19.

Methods

During March 11–December 15, 2021, adults admitted to 21 hospitals comprising the Influenza or Other Viruses in the Acutely Ill Network (IVY Network) and who received testing for SARS-CoV-2 were enrolled. The analysis comprised the timeframe during which SARS-CoV-2 Alpha (B.1.1.7) variant predominated (March–June 2021) followed by the SARS-CoV-2 Delta (B.1.617.2 and AY sublineages) variant (July–December 2021), and just before Omicron became the main circulating variant. VEs against COVID-19 hospitalization was evaluated for adults who received a single dose Ad26.COV2.S vaccine ≥14 days before illness onset. Methods have been described in detail elsewhere.[6,12–15] In brief, case-patients had COVID-19–like illness and received a positive SARS-CoV-2 test result (nucleic acid amplification test [NAAT] or antigen test) within 10 days of illness onset. Control patients were either "test-negative" controls hospitalized with signs or symptoms of an acute respiratory illness but testing negative for SARS-CoV-2 by NAAT, or "syndrome-negative" controls hospitalized without signs or symptoms of an acute respiratory illness and testing negative for SARS-CoV-2 by NAAT. Using standardized case report forms, interviews with patients or proxies were used to collect demographic and clinical

characteristics and electronic medical record (EMR) searches were performed to collect information about underlying medical conditions. Prior COVID-19 vaccination was verified primarily through source documentation (including state vaccination registries, EMRs, and vaccination record cards) and additionally through self-report including date and location of vaccination.

For patients hospitalized with COVID-19, we collected data on their clinical course until the outcome that occurred earliest: death, hospital discharge, or 28 days after hospital admission if still admitted. Disease severity was classified by dividing COVID-19 case patients into those who experienced death or required IMV (i.e., a composite measure we refer to as progression to high disease severity) and those who did not (i.e., no progression to high disease severity). Medical condition categories were defined using standardized definitions and obtained through electronic medical record (EMR) review by trained surveillance personnel. Persons with immunocompromising conditions were defined as those with one or more of the following: active solid organ cancer; active hematologic cancer (such as leukemia, lymphoma, or myeloma); HIV infection without AIDS; AIDS; congenital immunodeficiency syndrome; previous splenectomy; prior solid organ, stem cell, or bone marrow transplant; use of immunosuppressive medication; systemic lupus erythematosus; rheumatoid arthritis; psoriasis; scleroderma; or inflammatory bowel disease, including Crohn's disease or ulcerative colitis (Supplemental Table 1).

In this analysis of the effects of a single dose AD.26.COV2.S vaccine, participants who were vaccinated with a single dose AD.26.COV2.S vaccine and those who were unvaccinated were analyzed. Enrolled participants who received other vaccine products, such as an mRNA vaccine, or multiple doses of AD.26.COV2.S were excluded from this analysis. VEs against COVID-19–associated hospitalization was estimated using multivariable logistic regression, comparing the odds of being vaccinated with a single dose Ad26.COV2.S vaccine among case-patients versus controls, adjusting for potential confounders including admission date (biweekly intervals), geographic region (10 Health and Human Services

regions), age group (18–49, 50–64, or ≥65 years), sex, and self-reported race and Hispanic ethnicity. VEs was calculated as (1 – adjusted odds ratio) × 100%. Results were stratified by age group, presence of 0 vs ≥1 chronic medical conditions, presence of 0 vs ≥1 immunocompromising conditions, variant period (Alpha vs Delta), and time since receipt of the vaccine (14–90 days, 91–180 days, and >180 days post-vaccination). VEp against progression to high disease severity was estimated by restricting analysis to patients hospitalized with COVID-19. Here, we assessed the association between progression to death or IMV and prior vaccination with Ad26.COV2.S using multivariable logistic regression. These models adjusted for age group, sex, race and Hispanic ethnicity, and number of chronic medical conditions, and results were stratified by age group and presence of 0 versus ≥1 immunocompromising conditions. VEp was calculated as (1 – adjusted odds ratio) × 100%. Analyses were conducted using R (Vienna, Austria) and STATA (College Station, Texas). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy, e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

Results

A total of 12,524 adults were enrolled in the IVY study from March 11 through December 15, 2021. Of these, 6,316 were excluded because they met one or more exclusion criteria for the current analysis, most commonly because they received a mRNA vaccine product [n=6038] as a primary or booster dose. A total of 6,208 adults, including 3979 cases with laboratory-confirmed COVID-19 (5% vaccinated with Ad26.COV2.S) and 2229 controls without COVID-19 (13% vaccinated with Ad26.COV2.S, p<0.002) met inclusion criteria for this analysis. Compared with control patients, case patients were younger (median age [IQR]: 53 [40–64] vs 56 [42–66], p=0.002), more likely to be employed (48% vs 26%, p<0.001) and to be employed as a healthcare worker specifically (5% vs 3%, p=0.003) and less likely to be a long-term care facility resident (2% vs 4%, p<0.001), to have been hospitalized for any cause during the past year (24% vs 57%, p<0.001 to have ≥1 chronic medical condition (68% vs 85%, p<0.001), to currently use

tobacco (11% vs 28%, p<0.001), or to report a prior laboratory-confirmed SARS-CoV-2 infection (3% vs 12%, p<0.001). Median (IQR) number of days from vaccine dose 1 to illness onset was greater for case patients (140 [85–193]) compared with control patients (127 [69–183.p=0.0049) (Table 1).

VEs Against Hospitalization with COVID-19

Overall adjusted VEs (95% CI) for a single dose Ad26.COV2.S vaccine against COVID-19 hospitalization was 70% (63%–75%) and was lower in patients who were immunocompromised (55% [31%–72%]) than those who were immunocompetent (72% [64%–77%]). Among immunocompetent patients, VEs was higher (75% [67%–82%]) among patients aged 18-64 years than for those aged ≥65 years (66% [50%–77%]). VEs was similar between periods in which the Alpha variant (68% [43%–83%]) and Delta variant (72% [64%–78%]) predominated and remained similar 14–90 days (73% [60%–82%]), 91–180 days (71% [59%–80%]), and >180 days (70% [53%–81%]) post-vaccination. Finally, VEs was higher in patients without chronic medical conditions (86% [74%–93%]) than those with ≥1 chronic medical condition (64% [54%–73%]) (Figure 1, Supplementary Table 2).

VEp Against Progression to High Disease Severity

Of 3,979 COVID-19 case patients, 3,940 (95%) had complete data on clinical outcomes. Among these patients, COVID-19 patients vaccinated with a single dose Ad26.COV2.S vaccine were less likely to experience many severe clinical outcomes compared with unvaccinated COVID-19 patients, including invasive mechanical ventilation (18% vs 24%, p=0.0304), non-invasive ventilation (12% vs 17%, p=0.050), high-flow oxygen therapy (30% vs 40%, p=0.011), and vasopressor use (16% vs 23%, p=0.025). Vaccinated COVID-19 patients were less likely to experience high disease severity, defined as the composite of death or IMV, than unvaccinated COVID-19 patients (20% vs 27%, p=0.030) (Table 2). VEp (95% CI) was 36% (7%–56%) overall, and similar for immunocompetent patients (46% [18%–65%]),

patients aged 18–64 years (31% [11%–58%]) and patients aged ≥65 years (47% [4%–71%]). No VEp was observed among immunocompromised patients (-29% [-186%–42%]) (Figure 2, Supplementary Table 3).

Discussion

Vaccination with a single dose Ad26.COV2.S vaccine reduced the risk of COVID-19 hospitalization by more than two thirds; this was higher in immunocompetent persons compared with those who were immunocompromised. Protection against hospitalization was also sustained and stable through 6 or more months post-vaccination. Moreover, among patients hospitalized with COVID-19, prior vaccination with Ad26.COV2.S, compared with being unvaccinated, was associated with a lower risk of severe outcomes including a reduced composite risk of IMV or death.

The overall VEs against hospitalized COVID-19 observed in this analysis (70%) was similar to the vaccine efficacy against severe–critical COVID-19 (75%) demonstrated in a phase III randomized-controlled trial (RCT) of the 1-dose Ad26.COV2.S vaccine.[5] As severe outcomes are rare in clinical trials and adults with more severe underlying medical conditions are frequently under-represented in RCTs, results from this study and other post-marketing observational studies are critical to understanding the real-world effectiveness of COVID-19 vaccines. Importantly, among immunocompetent COVID-19 case-patients vaccination was associated with a lower risk (by 46%) of progressing to severe outcomes including death or IMV compared to unvaccinated patients. These results are largely consistent with a cohort study of US veterans that also found a substantial reduction in severe outcomes including death among Ad26.COV2.S vaccine recipients.[7] Although the VE estimates for Ad26.COV2.S are lower than those observed for mRNA COVID-19 vaccines,[6,11–14] the vaccine still provides substantial protection against severe COVID-19 with little waning for at least six months. Vaccines using Ad26-based vectors can be stored long-term either frozen or at 2–8 °C, enabling product distribution through existing vaccine supply chains. These vaccines have also been shown to be stable inside of syringes and needles, and when subjected to agitation or temperature excursions.[17] Importantly, real-world effectiveness of the

Ad26.COV2.S vaccine could still vary across regions based on pre-existing immunity to Ad26 and its effects on vaccine immunogenicity,[17] and further evaluation will be necessary.

The Ad26.COV2.S vaccine showed stable VE over time including among those patients >180 days from vaccination (100% of which became ill during the period of Delta variant predominance), suggesting stability of VE over the period pre-dating Omicron variant circulation and reinforcing that the protection for ≥6 months observed in clinical trials[5] generalizes to a real world setting with a high prevalence of medically complex patients. In addition, VEs for the Ad26.COV2.S vaccine was similar during the Delta-predominant period and Alpha-predominant periods, suggesting that protection was observed across two different SARS-CoV-2 variants,[18,19] although it may have been reduced against Omicron given the reduced effectiveness observed for mRNA vaccines.[20] Although a second dose of Ad26.COV2.S, or alternatively, an mRNA vaccine, ≥2 months from the first dose is now recommended for recipients of the Ad26.COV2.S vaccine,[17,21] our results showed that a single dose Ad26.COV2.S vaccine remained reasonably effective against the Delta variant over time from vaccination and across periods of different variant predominance. This minimal waning observed here reinforces preexisting evidence of durable humoral and cellular immune responses to ad26 vaccines, which use a non-replicating viral vector that enters the nucleus of cells to induce an immune response.[22]

We also found that Ad26.COV2.S vaccination attenuated the likelihood of progression to severe disease among those who were hospitalized with COVID-19 despite vaccination. While VEp against progression to high disease severity was substantial for immunocompetent persons (46%), the Ad26.COV2.S vaccine appeared ineffective in preventing progression to high severity in immunocompromised patients. Data are lacking on differences in disease attenuation between immunocompromised and immunocompetent populations. However, a growing body of literature suggests that immunocompromised patients, including transplant recipients and patients with cancer, have diminished humoral and cellular immune responses to mRNA and inactivated SARS-CoV-2 vaccines.[23–25]

Our results suggest that the immune response to a single dose Ad26.COV2.S vaccine among immunocompromised patients may be insufficient to attenuate disease severity in patients who have been hospitalized with COVID-19.

Our findings must be considered in the context of several limitations. First, this analysis focused exclusively on protection from a single dose of the Ad26.COV2.S vaccine and did not evaluate multiple doses of the vaccine or the Ad26.COV2.S vaccine combined with mRNA vaccine doses. Additional doses of vaccine would likely increase vaccine effectiveness.[17,21] Second, while we found overall lower VE for patients with immunocompromising conditions, this analysis was not powered to look at VE for specific immunocompromising conditions. Third and relatedly, it is possible that the types of immunocompromising conditions reported among patients included in this analysis who received the Ad26.COV2.S vaccine were different than those who received mRNA vaccines (i.e., due to different vaccine indications for different conditions) and could have affected VEs and VEp for this subgroup. Fourth, while we did not assess for waning of VE over time since vaccination within periods of different variant predominance, no meaningful decline in VE was observed for either metric. Fifth, VE associated with newly emergent variants was not assessed. Sixth, VE was not assessed against SARS-CoV-2 infection or mild illness. Finally, although VE estimates were adjusted for relevant potential confounders, residual confounding is possible.

Conclusions

A single dose Ad26.COV2.S vaccine provided substantial protection against severe COVID-19 throughout 2021 in this real-world observational study, consistent with vaccine efficacy reported in clinical trials of Ad26.COV2.S conducted in 2020. Although the observed vaccine effectiveness for Ad26.COV2.S was lower than that described for mRNA COVID-19 vaccines, a single dose of Ad26.COV2.S did result in strong protection against severe COVID-19 for at least 6 months in immunocompetent populations. The

Ad26.COV2.S vaccine is an important alternative to mRNA COVID-19 vaccines for those who are unable to receive an mRNA vaccine.

NOTES

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Potential conflicts

M Gaglani: CDC: BSWH US Flu/COVID VE Newtork, HAIVEN, Synergy studies; CDC-Abt: BSWH FluVax Trial and RECOVER-PROTECT Cohort Studies; CDC-Westat: BSWH VISION COVID-Flu VE Study; Janssen: BSWH RSV Severity App Birth Cohort Study; Co-Chair of Infectious Diseases and Immunization Committee – Texas Pediatric Society – Texas Chapter of American Academy of Pediatrics; **A Ginde:** NIH, Department of Defense; Faron Pharmaceuticals; AbbVie; D Douin: NIH/NIGMS Institutional Training Grant; **J Casey:** NIH and Department of Defense grants unrelated to this work; **T McNeal:** Panelist for Society of Hospital Medicine Updates in Heart Failure; Board member for Scott & White Clinic Physicians Board of Directors; **K Gibbs:** NECTAR Executive Committee member ACTIV4-HT; **DC Files:** Cytovale consulting fees; Medpace Data Safety Monitoring Board; **DN Hager:** NIHLBI participant in the ACTIV4d-Host Tissue Trial; Chair DSMD – SAFE EVICT Trial of VIT C in COVID-19; **MN Gong:** Grants from NHLBI and AHRQ; Consulting fees for Endpoint for scientific advisory panel; Honoraria – Medicine Grand Rounds from Westchester Medical Center; Support for attending ATS Board of Directors meeting; DSMB for Regeneron study and REPLENISH trial; **NJ Johnson:** NIH grants paid to University of Washington Royalty Research Fund;

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Table 1. Characteristics of Patients Vaccinated with One Dose of Ad26.COV2.S (Johnson & Johnson), COVID-19 Case Patients and Control Patients, IVY Network

Characteristic, n/N (%)	Total (n=6208)	Case Patients (n=3979)	Control Patients (n=2229)	P-value
Clinical Group				
Vaccinated with One Dose of Ad26.COV2.S	478/6208 (7.7)	192/3979 (4.8)	286/2229 (12.8)	<0.001
Age in years				
Median (IQR)	54 (41–65)	53 (40–64)	56 (42–66)	0.002
18–49 years	2481/6208 (40.0)	1638/3979 (41.2)	843/2229 (37.8)	0.006
50–64 years	2103/6208 (33.9)	1348/3979 (33.9)	755/2229 (33.9)	
≥65 years	1624/6208 (26.2)	993/3979 (25.0)	631/2229 (28.3)	
Female sex	2939/6208 (47.3)	1873/3979 (47.1)	1066/2229 (47.8)	0.569
Race/ethnicity[b]				
Non-Hispanic White	3208/6208 (51.7)	1985/3979 (49.9)	1223/2229 (54.9)	<0.001
Non-Hispanic Black	1515/6208 (24.4)	937/3979 (23.5)	578/2229 (25.9)	
Hispanic, any race	1083/6208 (17.4)	787/3979 (19.8)	296/2229 (13.3)	
Non-Hispanic, all other races	286/6208 (4.6)	192/3979 (4.8)	94/2229 (4.2)	
Unknown	116/6208 (1.9)	78/3979 (2.0)	38/2229 (1.7)	
US Census Region[c]				
Northeast	894/6208 (14.4)	592/3979 (14.9)	302/2229 (13.5)	0.407
South	2565/6208 (41.3)	1624/3979 (40.8)	941/2229 (42.2)	
Midwest	1451/6208 (23.4)	922/3979 (23.2)	529/2229 (23.7)	
West	1298/6208 (20.9)	841/3979 (21.1)	457/2229 (20.5)	
LTCF Resident	159/5963 (2.7)	76/3821 (2.0)	83/2142 (3.9)	<0.001
Employed	1987/4959 (40.1)	1513/3126 (48.4)	474/1833 (25.9)	<0.001
Healthcare worker	222/4959 (4.5)	161/3126 (5.2)	61/1833 (3.3)	0.003
≥1 previous hospitalization in the last year	2075/5714 (36.3)	882/3633 (24.3)	1193/2081 (57.3)	<0.001
≥1 chronic medical condition[d]	4619/6207 (74.4)	2716/3978 (68.3)	1903/2229 (85.4)	<0.001
Current tobacco use	935/5345 (17.5)	382/3382 (11.3)	553/1963 (28.2)	<0.001
Self-reported previous laboratory-confirmed SARS-	381/6207(6.1)	108/3978 (2.7)	273/2229 (12.2)	<0.001

CoV-2 infection				
Days from vaccine dose 1 to illness onset, median (IQR)	135 (75-185)	140 (84.5-193)	126.5 (69-183)	0.049

Data are No./total No. (%) except where indicated.

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; LTFC, long-term care facility; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Hospitals by region were Northeast: Baystate Medical Center (Springfield, MA), Beth Israel Deaconess Medical Center (Boston, MA), Montefiore Medical Center (Bronx, NY); South: Vanderbilt University Medical Center (Nashville, TN), University of Miami Medical Center (Miami, FL), Emory University Medical Center (Atlanta, GA), Johns Hopkins Hospital (Baltimore, MD), Wake Forest University Baptist Medical Center (Winston-Salem, NC), Baylor Scott and White Health (Temple, TX); Midwest: University of Iowa Hospitals and Clinics (Iowa City, IA), University of Michigan Hospital (Ann Arbor, MI), Hennepin County Medical Center (Minneapolis, MN), Barnes-Jewish Hospital (St Louis, MO), Cleveland Clinic (Cleveland, OH), Ohio State University Wexner Medical Center (Columbus, OH); West: Stanford University Medical Center (Stanford, CA), UCLA Medical Center (Los Angeles, CA), UCHealth University of Colorado Hospital (Aurora, CO), Oregon Health and Science University Hospital (Portland, OR), Intermountain Medical Center (Murray, UT), University of Washington (Seattle, WA).

[b]Racial and ethnic groups were reported by the patient or proxy.

[c]Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

[d]Chronic medical conditions were obtained through medical chart review by trained personnel and classified by condition category specified in the table; a full list of conditions is included in Supplementary Table 1.

FIGURE LEGENDS

Figure 1. Vaccine Effectiveness Against Susceptibility to COVID-19 Hospitalization (VEs) for Single Dose Ad26.COV2.S (Johnson & Johnson) COVID-19 Vaccine Overall and by Subgroups, IVY Network[a]

[a]Vaccine effectiveness models for immunocompetency, variant period, time since vaccination, and conditions were adjusted for admission date (in biweekly intervals), US Health and Human Services Region, self-reported race and Hispanic ethnicity, age (18-49, 50-64, and ≥65 years of age), and sex. The model for age group adjusted for age in years as a continuous variable.

Figure 2. Vaccine Effectiveness Against Progression to Invasive Mechanical Ventilation or to Death within 28 days (VEp) for Single Dose Ad26.COV2.S (Johnson & Johnson) COVID-19 Vaccine Among Adults Hospitalized With COVID-19, IVY Network[a]

[a]Vaccine effectiveness models adjusted for age, sex, race and Hispanic ethnicity, and number of underlying medical conditions (as 0, 1, 2, 3, or ≥4 categories of conditions). The model for age group adjusted for age in years as a continuous variable.

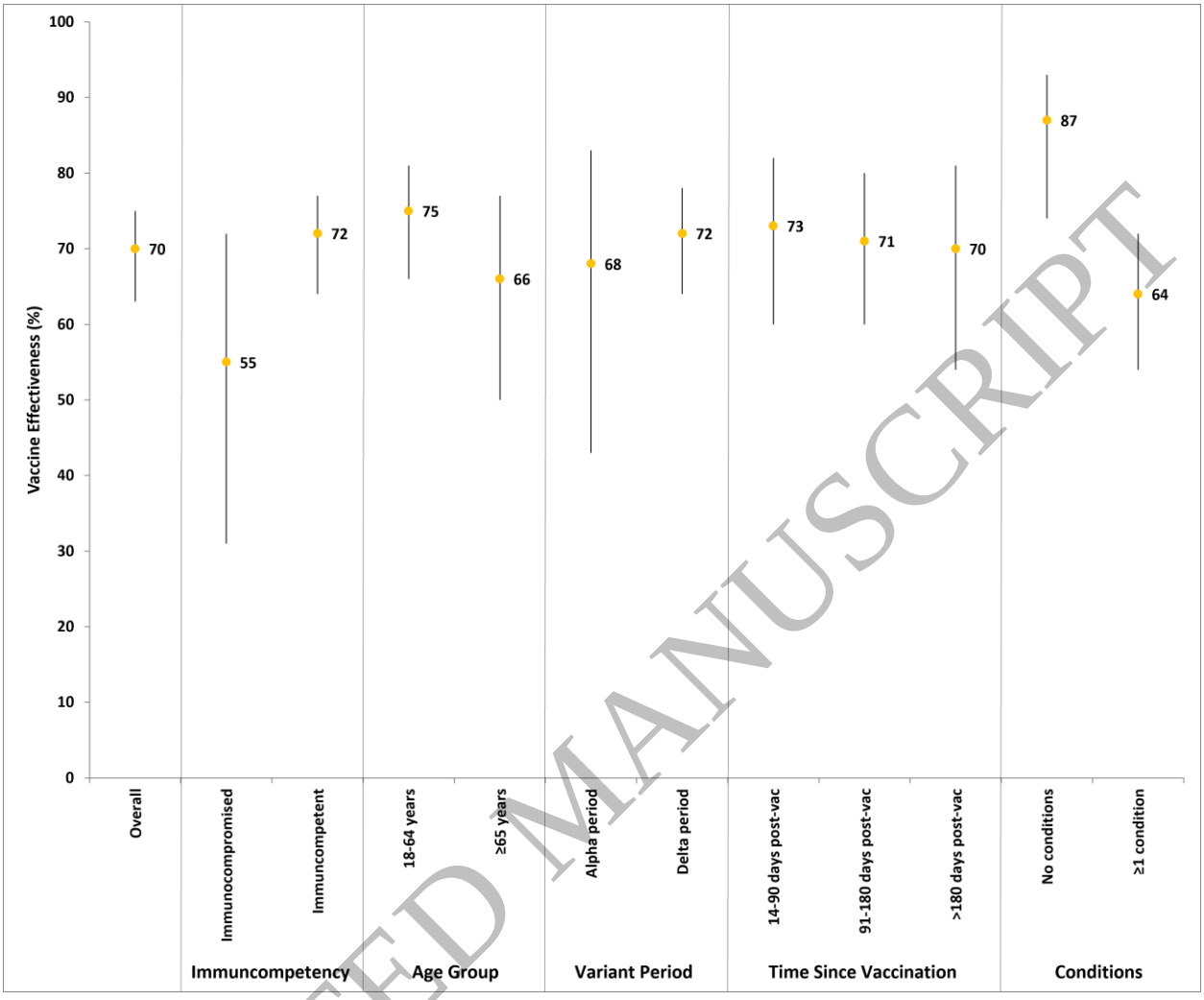
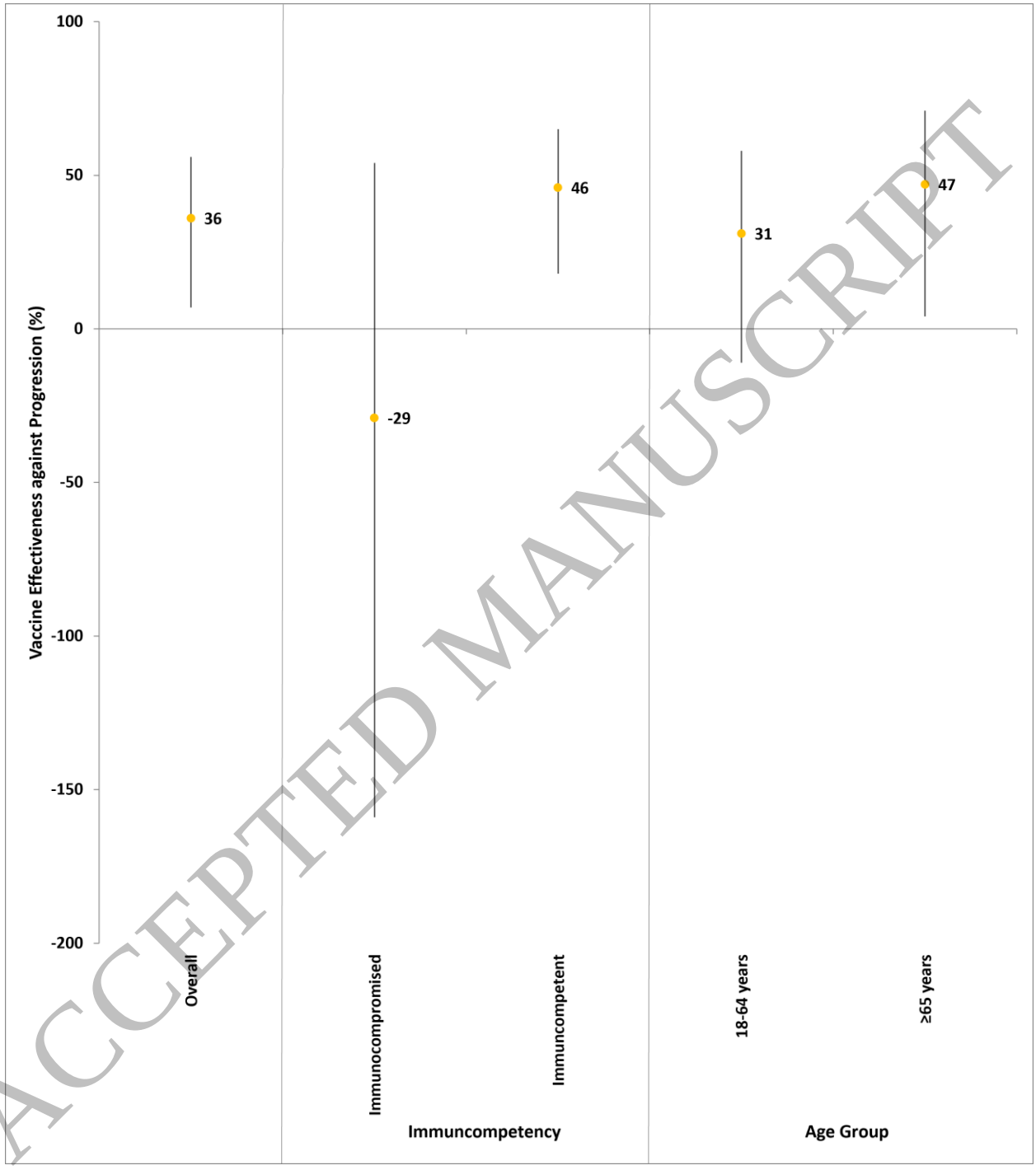


Figure 1
165x136 mm (.60 x DPI)

1 s



2

3 **Figure 2**
4 **165x186 mm (.60 x DPI)**