With vaccination rates lagging in areas with higher social vulnerability, small financial incentives should be considered in conjunction with other equity-promoting strategies.[5,6] The social incentive of cash cards for drivers may also encourage people to help get their friends and family vaccinated, a powerful motivator for those undecided about vaccination. With hundreds of millions of dollars being spent to accelerate COVID-19 vaccine uptake, these study findings suggest that this strategy for increasing vaccination merits greater investment.

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Age- and Sex-Specific Incidence of Cerebral Venous Sinus Thrombosis Associated With Ad26.COV2.S COVID-19 Vaccination

Recent reports[1-4] suggest a possible association between Ad26.COV2.S (Johnson & Johnson/Janssen) COVID-19 vaccination and cerebral venous sinus thrombosis (CVST). Estimates of postvaccination CVST risk require accurate age- and sex-specific prepandemic CVST incidence rates; however, reported rates vary widely.[5] We compared the age- and sex-specific CVST rates after Ad26.COV2.S vaccination with the prepandemic CVST rate in the population.

Supplemental content

Methods | In this population-based cohort study, to estimate the risk of CVST after Ad26.COV2.S vaccination, we first identified all incident cases of CVST in Olmsted County, Minnesota from January 1, 2001, through December 31, 2015 (eMethods in the Supplement). Sex-and age-adjusted incidence rates were adjusted to the 2010 US census population. We used CDC Vaccine Adverse Event Reporting System (VAERS) data from February 28, 2021 (vaccine approval date) to May 7, 2021, to estimate the incidence of CVST after Ad26.COV2.S vaccination assuming 3 (15, 30, and 92 days) plausible postvaccination periods during which individuals were considered to be at risk of CVST. We then compared post-Ad26.COV2.S vaccination CVST rates with prepandemic rates to estimate postvaccination CVST risk. This study was approved by the Mayo Clinic institutional review board. Medical records of Olmsted County residents with CVST were reviewed only if the residents had signed an authorization for accessing their medical records for research purposes. SAS, version 9.4 (SAS Institute Inc) and R, version 4.0.3 (R Project for Statistical Computing) were used for statistical analyses. Significance was set at a 2-sided $P < .05$.

Results | From 2001 through 2015, 39 Olmsted County residents developed acute incident CVST. A total of 29 patients (74.4%) had a predisposing venous thromboembolism risk factor (eg, infection, active cancer, or oral contraceptives [for women]) within 92 days before the event. The median age at diagnosis was 41 years (range, 22-84 years); 22 residents with CVST (56.4%) were female. The overall age- and sex-adjusted CVST incidence was 2.34 per 100 000 person-years (PY) (95% CI, 1.60-3.08 per 100 000 PY). Age-adjusted CVST rates for female and male individuals were 2.46 per 100 000 PY (95% CI, 1.43-3.49 per 100 000 PY) and 2.34 per 100 000 PY (95% CI, 1.22-3.46 per 100 000 PY), respectively. Men aged 65 years or older had the highest CVST rate (6.22 per 100 000 PY; 95% CI, 2.50-12.82 per 100 000 PY), followed by women aged 18 to 29 years (4.71 per 100 000 person-years; 95% CI, 2.26-8.66 per 100 000 PY) (**Table 1**).

Table 1. Annual Incidence of CVST Among Residents of Olmsted County, Minnesota, From 2001 to 2015 by Age and Sex

Sex and age, y	CVST cases, No.	Population, person-years	Incidence, per 100 000 person-years (95% CI)
Female			
18-29	10	212 441	4.71 (2.26-8.66)
30-39	4	156 541	2.56 (0.70-6.54)
40-49	2	157 433	1.27 (0.15-4.59)
50-64	4	195 110	2.05 (0.56-5.25)
≥65	2	148 204	1.35 (0.16-4.88)
Total	22	869 729	2.53 (1.59-3.83)
Age-adjusted rate[a]	NA	NA	2.46 (1.43-3.49)
Male			
18-29	2	181 342	1.10 (0.13-3.99)
30-39	3	147 386	2.04 (0.42-5.95)
40-49	2	145 879	1.37 (0.16-4.96)
50-64	3	175 760	1.71 (0.35-4.99)
≥65	7	112 508	6.22 (2.50-12.82)
Total	17	762 875	2.23 (1.30-3.57)
Age-adjusted rate[a]	NA	NA	2.34 (1.22-3.46)
All			
18-29	12	393 783	3.05 (1.57-5.32)
30-39	7	303 927	2.30 (0.92-4.74)
40-49	4	303 312	1.32 (0.36-3.38)
50-64	7	370 870	1.89 (0.76-3.89)
≥65	9	260 712	3.45 (1.58-5.53)
Total	39	1 632 604	2.39 (0.61-1.67)
Age-adjusted rate[a]	NA	NA	2.38 (1.63-3.13)
Age- and sex-adjusted rate[a]	NA	NA	2.34 (1.60-3.08)

Abbreviations: CVST, cerebral venous sinus thrombosis; NA, not applicable.

[a] Adjusted to the US census 2010 population.

As of May 7, 2021, 8 727 851 Ad26.COV2.S vaccine doses had been administered in the US; 46 potential CVST events occurring within 92 days after Ad26.COV2.S vaccination were reported to VAERS. Eight events were excluded because they were potentially duplicate reports (4) or were not objectively diagnosed (4). Twenty-seven of 38 objectively diagnosed cases of CVST after Ad26.COV2.S vaccination (71.1%) occurred in female individuals. The median patient age was 45 years (range, 19-75 years). The median time from vaccination to CVST was 9 days (IQR, 6-13 days; range, 1-51 days); 31 of 38 cases of CVST (81.6%) occurred within 15 days after vaccination, and 36 (94.7%) occurred within 30 days.

The overall incidence rate of post-Ad26.COV2.S vaccination CVST was 8.65 per 100 000 PY (95% CI, 5.88-12.28 per 100 000 PY) at 15 days, 5.02 per 100 000 PY (95% CI, 3.52-6.95 per 100 000 PY) at 30 days, and 1.73 per 100 000 PY (95% CI, 1.22-2.37 per 100 000 PY) at 92 days (**Table 2**). The 15-day postvaccination CVST incidence rates for female and male individuals were 13.01 per 100 000 PY (95% CI, 8.24-19.52 per 100 000 PY) and 4.41 per 100 000 PY (95% CI, 1.90-8.68 per 100 000 PY), respectively. The postvaccination CVST rate among females was 5.1-fold higher compared with the pre-COVID-19 pandemic rate (13.01 vs 2.53 per 100 000 PY; $P < .001$) (Table 2). This risk was highest among women aged 40 to 49 years (29.50 per 100 000 PY; 95% CI, 13.50-55.95 per 100 000 PY), followed by women aged 30 to 39 years (26.50 per 100 000 PY; 10.65-54.63 per 100 000 PY).

Discussion | In this population-based cohort study, we found that the CVST incidence rate 15 days after Ad26.COV2.S vaccination was significantly higher than the prepandemic rate. However, the higher rate of this rare adverse effect must be considered in the context of the effectiveness of the vaccine in preventing COVID-19 (absolute reduction of severe or critical COVID-19 of 940 per 100 000 PY).[6]

Most CVST events occurred within 15 days after vaccination, which is likely the highest at-risk period. The postvaccination CVST rate among females was higher than the prepandemic rate among females. The highest risk was among women aged 30 to 49 years, but the absolute CVST risk was still low in this group (up to 29.5 per 100 000 PY among women aged 40-49 years). The reason that women had a higher incidence of postvaccination CVST is unclear; concomitant CVST risk factors or autoantibody production might have been involved.[2] The overall prepandemic CVST incidence rate was slightly higher in our study than in other studies (0.22-1.57 per 100 000 PY)[5] likely because we captured all objectively diagnosed incident CVST cases in a well-defined population, including those discovered at autopsy.

The present study avoided referral bias and included only objectively diagnosed and confirmed cases. Only cases with adequate details or imaging findings reported on VAERS were used. Study limitations include possible ascertainment bias by including only objectively diagnosed CVST cases. VAERS reporting is voluntary and subject to reporting

Table 2. Incidence Rate of CVST Occurring After the Administration of the Ad26.COV2.S Vaccine

Risk period, sex, and age, y	Observed CVST cases, No.	Doses administered, No.	Person-years at risk	Incidence, per 100 000 person-years (95% CI)	Expected CVST cases, No.[a]	Incidence rate ratio (95% CI)[b]	*P* value[c]
15 d							
Female							
18-29	2	641 510	26 346	7.59 (0.91-27.40)	1.24	1.61 (0.17-7.57)	.63
30-39	7	642 745	26 397	26.52 (10.65-54.63)	0.67	10.38 (2.64-48.33)	<.001
40-49	9	743 256	30 525	29.48 (13.50-55.95)	0.39	23.21 (4.80-221.05)	<.001
50-64	5	1 463 416	60 101	8.32 (2.70-19.42)	1.23	4.06 (0.87-20.45)	.04
≥65	0	814 947	33 469	0.00 (0.00-11.03)	0.45	0.00 (0.004-23.58)	>.99
Total	23	4 305 874	176 837	13.01 (8.24-19.52)	4.47	5.14 (2.74-9.68)	<.001
Male							
18-29	1	714 458	29 342	3.41 (0.10-18.98)	0.32	3.09 (0.05-59.36)	.36
30-39	0	728 699	29 927	0.00 (0.00-12.33)	0.61	0.00 (0.00-11.92)	>.99
40-49	3	775 390	31 844	9.42 (1.95-27.54)	0.44	6.87 (0.79-82.34)	.04
50-64	3	1 505 505	61 829	4.85 (1.00-14.18)	1.06	2.84 (0.38-21.32)	.19
≥65	1	697 925	28 663	3.49 (0.10-19.43)	1.78	0.56 (0.01-4.36)	>.99
Total	8	4 421 977	181 606	4.41 (1.90-8.68)	4.05	1.98 (0.74-4.83)	.12
30 d							
Female							
18-29	2	641 510	52 692	3.80 (0.46-13.70)	2.48	0.81 (0.09-3.78)	>.99
30-39	8	642 745	52 794	15.15 (6.53-29.85)	1.35	5.93 (1.59-26.93)	.003
40-49	10	743 256	61 049	16.38 (7.86-30.12)	0.78	12.89 (2.75-120.81)	<.001
50-64	6	1 463 416	120 202	4.99 (1.83-10.87)	2.46	2.43 (0.58-11.73)	.20
≥65	0	814 947	66 938	0.00 (0.00-5.51)	0.90	0.00 (0.00-11.79)	>.99
Total	26	4 305 874	353 675	7.35 (4.80-10.77)	8.95	2.91 (1.58-5.38)	<.001
Male							
18-29	1	714 458	58 684	1.70 (0.05-9.49)	0.65	1.55 (0.03-29.68)	.56
30-39	0	728 699	59 854	0.00 (0.00-6.17)	1.22	0.00 (0.00-5.96)	.56
40-49	3	775 390	63 689	4.71 (0.97-13.77)	0.87	3.44 (0.39-41.17)	.16
50-64	5	1 505 505	123 659	4.04 (1.31-9.44)	2.11	2.37 (0.46-15.26)	.29
≥65	1	697 925	57 326	1.74 (0.05-9.72)	3.57	0.28 (0.01-2.18)	.28
Total	10	4 421 977	363 211	2.75 (1.32-5.06)	8.09	1.24 (0.51-2.86)	.54
92 d							
Female							
18-29	2	641 510	161 589	1.24 (0.15-4.47)	7.61	0.26 (0.03-1.23)	.08
30-39	8	642 745	161 901	4.94 (2.13-9.73)	4.14	1.93 (0.52-8.78)	.39
40-49	10	743 256	187 218	5.34 (2.56-9.82)	2.38	4.20 (0.90-39.39)	.05
50-64	6	1 463 416	368 619	1.63 (0.60-3.54)	7.56	0.79 (0.19-3.82)	.75
≥65	1	814 947	205 276	0.49 (0.01-2.71)	2.77	0.36 (0.01-6.93)	.58
Total	27	4 305 874	1 084 603	2.49 (1.64-3.62)	27.44	0.98 (0.54-1.81)	>.99
Male							
18-29	1	714 458	179 964	0.56 (0.02-3.10)	1.98	0.50 (0.01-9.68)	>.99
30-39	0	728 699	183 551	0.00 (0.00-2.01)	3.74	0.00 (0.00-1.94)	.09
40-49	3	775 390	195 312	1.54 (0.32-4.49)	2.68	1.12 (0.13-13.43)	>.99
50-64	6	1 505 505	379 220	1.58 (0.58-3.44)	6.47	0.93 (0.20-5.72)	>.99
≥65	1	697 925	175 800	0.57 (0.02-3.17)	10.94	0.09 (0.00-0.71)	.007
Total	11	4 421 977	1 113 848	0.99 (0.49-1.77)	24.82	0.44 (0.19-1.00)	.05

Abbreviation: CVST, cerebral venous sinus thrombosis.

[a] Based on the population of Olmsted County, Minnesota.

[b] Observed vs expected.

[c] The exact binomial test *P* value was calculated using the binom.test() function in the R, version 4.0.3, with the probability of an observed CVST case being calculated as K2/(K1+K2), where K1 was the number of prepandemic CVST cases in the general population (expected) and K2 was the number of postvaccination CVST cases (observed).

biases. VAERS monitors vaccine adverse events but does not prove causality.

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Payer-Specific Negotiated Prices for Prescription Drugs at Top-Performing US Hospitals

Nearly one-third of pharmaceutical spending in the US is for clinician-administered drugs (eg, infusions).[1] Medicare Part B reimbursement for these drugs is set at the average sales price (ASP)—the average price charged by manufacturers to wholesalers net of any rebates or discounts—plus a 6% markup (or 4.3% during budget sequestration). By contrast, hospitals and physician offices charge commercial insurers whatever price they negotiate, and they retain any difference between the negotiated price and cost of acquisition.

Supplemental content

While these negotiated prices have long been confidential, a transparency rule that took effect on January 1, 2021, requires hospitals to post payer-specific negotiated prices for all items and services, including clinician-administered drugs. We analyzed a set of top-performing hospitals to quantify drug pricing variation across insurers.

Methods | We searched the websites of the 20 top-rated hospitals by *US News and World Report* rankings for pricing files from January 1 through September 15, 2021. We selected these hospitals because they were likely to have sufficient resources to comply with reporting requirements and would serve as a model for other hospitals that were deciding on how to comply (eTable 1 in the Supplement). We extracted commercial insurer-negotiated prices and self-pay cash prices (the discounted prices for patients paying without insurance) for the 10 drugs with the highest 2019 Medicare Part B expenditures (eTable 2 in the Supplement).[2] We evaluated median prices relative to the Medicare payment limit to enable comparisons of hospital markups across drugs. We used Stata, release 16.1 (StataCorp LLC) and Excel, version 16.16.27 (Microsoft) for the study analysis, which was performed from July 1 to September 15, 2021. Institutional review board approval was not required because we used only publicly available data on prices of prescription drugs and did not use patient information.

Results | Seventeen of the 20 hospitals (85%) posted files aimed at complying with the new transparency rule. Eleven (55%) included payer-specific pharmaceutical prices. Of the hospitals that released pharmaceutical data, 82% (and 85% of hospitals overall) were 340B entities, which entitled them to acquire drugs from manufacturers at prices below the ASP.[3]

Prices varied between and within hospitals (**Figure**). Median negotiated prices for the 10 drugs in the study sample ranged from 169% (IQR, 137%-264%) of the Medicare payment limit at Rush University Medical Center to 344% (IQR, 307- 368%) at the Mayo Clinic Hospital-Arizona, and median self-pay cash prices ranged from 149% (IQR, 124%-203%) of the Medicare payment limit at Rush to 306% at Brigham and Women's Hospital (IQR, 273%-327%) and Massachusetts General Hospital (IQR, 283%-327%; **Table**). There was also substantial variation by drug, with the lowest median negotiated prices relative to the Medicare payment limit observed for abata-