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COVID-19 Vaccination Hesitancy and Its Association With Altered Presentation of Primary Rhegmatogenous Retinal Detachment



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- **PURPOSE:** Evaluate factors associated with coronavirus 2019 (COVID-19) vaccine hesitancy and clinical trends in primary rhegmatogenous retinal detachments (RRDs) during the first year of vaccine availability.
- **DESIGN:** Single-center, clinical cohort study.
- **METHODS:** Consecutive patients from December 14, 2020, to December 12, 2021, presenting vaccinated (Prior-), subsequently vaccinated (Later-), or remaining unvaccinated (Never-Vax). Primary outcome was proportion with macula-off (mac-off) RRD. Secondary outcomes included logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA), primary proliferative vitreoretinopathy (PVR), proportion lost to follow-up, and distance traveled.
- **RESULTS:** 1047 patients were divided into 391 Prior-, 252 Later-, and 404 Never-Vax cohorts. Significantly greater proportions of Later- and Never-Vax cohorts presented with mac-off RRDs (Prior-Vax = 44.5%; Later-Vax = 54%, $P < .0001$; Never-Vax = 57.9%, $P < .0001$) and primary PVR (Prior-Vax = 4.3%; Later-Vax = 13.6%, $P < .0001$; Never-Vax = 17.1%, $P < .0001$) compared to Prior-Vax cohort. Significantly greater proportion of Never-Vax cohort (7.7%, $P < .0001$) were lost to follow-up compared to Prior- (2.3%) and Later-Vax (2.2%) cohorts. Never-Vax cohort (median = 35 miles) traveled farther compared to Prior- (median = 22.3 miles; $P < .0001$) and Later-Vax cohorts (25.45 miles; $P = .0038$). Prior-Vax cohort had significantly better ($P < .05$) initial (median = 0.30 logMAR) and final (0.18 logMAR) BCVA compared to Later- (Initial: 0.54 logMAR; Final: 0.30 logMAR) and Never-Vax (Initial: 0.70 logMAR; Final: 0.40 logMAR) cohorts.
- **CONCLUSIONS:** COVID-19 vaccine hesitancy is associated with worse clinical presentation and outcomes for primary RRD. (Am J Ophthalmol 2022;242: 7–17. © 2022 Elsevier Inc. All rights reserved.)

P RIMARY RHEGMATOGENOUS RETINAL DETACHMENT (RRD) is an urgent medical condition and typically warrants prompt surgical intervention, especially if the subretinal fluid (SRF) spares the macula (mac-on).^{1,2} Progression to involve the fovea (mac-off) has been shown to result in worse visual outcomes even after successful surgical repair.¹ Previous studies highlighted a significant delay in intervention of urgent and emergent ophthalmic diseases such as RRD during the coronavirus disease 2019 (COVID-19) pandemic due to challenges posed by a decline in healthcare access, socioeconomic hardship, and general anxiety.³⁻⁸ This has prompted the development of safe and effective COVID-19 vaccines with the aim of suppressing the virus and restoring social and economic normality.

Three COVID-19 vaccines are currently approved for use in the United States, including 2 mRNA vaccines requiring 2-dose series (Pfizer-BioNTech [Pfizer]⁹ and Moderna¹⁰) and a single-dose viral vector vaccine (Janssen-Johnson & Johnson [J&J]¹¹). Although the initial scarcity of vaccines necessitated a phased approach to prioritize essential personnel and high-risk populations, vaccination of the general US population began on March 30, 2021, once supply became more readily available.¹² Subsequently, the age limit for the Pfizer vaccine was expanded to include children ages 5-15 years.

Vaccine hesitancy, defined by the World Health Organization (WHO) as a delay or refusal of immunization when it is available, is considered a top 10 threat to global health.¹³ With the general anxiety brought about by the pandemic, numerous studies have shown a delay in ophthalmic care and worse clinical outcomes for patients with ophthalmic emergencies such as RRDs.⁵⁻⁸ Our aim was to evaluate and describe the factors associated with COVID-19 vaccine hesitancy and the clinical trends for primary RRDs at presentation, treatment course, and clinical outcomes in the Upper Midwest region of the United States (US) during the first full year after the vaccines became available.

METHODS

Retrospective cohort study was conducted adhering to tenets of Declaration of Helsinki and to US Health Insur-

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ance Portability and Accountability Act of 1996 with institutional review board approval by Allina Healthcare (Reference no. 1881491). This study was HIPAA-compliant and conducted at a multiprovider, multilocation single-subspecialty institution (Vitreoretinal Surgery, PLLC) in metropolitan Minneapolis and St Paul (MSP) with satellite offices in Duluth and St Cloud in Minnesota.

Billing data from 52 weeks beginning on December 14, 2020 (first vaccine was administered in Minnesota on December 15¹⁴), through December 12, 2021, were queried for frequency of billed *Current Procedural Terminology* (CPT) codes 67107 (scleral buckle [SB]), 67108 (pars plana vitrectomy [PPV] or combination of SB/PPV), 67110 (pneumatic retinopexy [PR]), and 67113 (repair of complex RD). Patients with previous RRD repair in same eye, who had ocular trauma, or with nonrhegmatogenous etiology were excluded. Only first eye was included in patients with bilateral RRDs during this period.

Patients were considered vaccinated after a single dose of J&J vaccine or at least 1 dose of Pfizer or Moderna vaccine. Vaccination status was noted as “Prior-Vax” if patients were vaccinated prior to initial presentation. Those unvaccinated at initial presentation were separated into “Later-Vax” or “Never-Vax” cohorts depending on if they received vaccination or remained unvaccinated during postoperative course, respectively. Prior-Vax status was confirmed with perioperative records. Later- and Never-Vax statuses were self-reported and confirmed with documentation when available. Patients who had a documented contraindication to receiving vaccination at the time of initial presentation were excluded. Furthermore, those who presented unvaccinated prior to and without a follow-up appointment after March 30, 2021 (when eligibility was expanded to general population), were excluded because of unknown Later- or Never-Vax status.

Of 285 patients treated prior to general vaccine availability (December 14, 2020, to March 29, 2021), 4.21% (12 patients) had unknown vaccination statuses and were excluded. For the remaining patients, 57 obtained early vaccination, 107 obtained vaccinations on or after March 30, 2021, and 109 declined. Because the vaccination rate for this cohort (60.1%) was similar to that seen after March 30, 2021 (61.6%; 477 vaccinated, 297 unvaccinated), they were included for analysis.

Demographic, preoperative, intraoperative, and follow-up data were collected. Race was self-identified as Caucasian, Black, Asian, Native American, Hispanic, Decline to Specify, or Other. Median household income was used as a quantitative surrogate for socioeconomic status tabulated from American Communities Survey 2017 of median income by the patient home zip code.^{6,8,15} Patients were considered “established” if previously seen within a 3-year period before diagnosis; otherwise, they were considered “new.”

Distance from patient home zip code to clinic was used as a quantitative surrogate for health care access and was

calculated based on the shortest route (miles) using Google Maps (Alphabet, Inc). Time between initial diagnosis and surgery was recorded. Initial Snellen best-corrected visual acuity (BCVA) was obtained from the first visit when the patient received the diagnosis. Final BCVA was determined at the latest postoperative visit; however, those with a follow-up course less than 3 months were excluded.

Primary outcome was proportion of vaccinated vs unvaccinated patients demonstrating mac-on RRD, as opposed to mac-off RRD (defined as foveal detachment) on preoperative evaluation. Secondary outcomes include initial and final BCVA, proportion with symptom duration of 1 day or less, mean duration of symptoms, time to surgical repair, and presence of grade C or higher primary proliferative vitreoretinopathy (PVR).

Statistical analysis was performed on JMP software (SAS Institute, Cary, NC). Snellen BCVA was converted to logarithm of the minimum angle of resolution (logMAR) units for quantitative analysis, with logMAR values for BCVA of light perception, hand motion, and counting fingers assigned 2.7, 2.3, and 1.8, respectively.¹⁶ Comparison of categorical variables between the 2 cohorts was completed using a 2-tailed Fisher exact test. Continuous quantitative variables including age, median household income, travel distance, duration of symptoms, time to surgery, and logMAR BCVA were found to be nonnormal using the Shapiro-Wilk test. The Median test, using median rank scores, was used for comparisons involving travel distance and logMAR BCVA. All other nonnormal distributions were compared using the Mann-Whitney *U* test. *P* value <.05 was considered statistically significant.

RESULTS

• **BASELINE CHARACTERISTICS:** Our study population was divided into cohorts based on COVID-19 vaccination status, defined as receiving at least 1 dose of Pfizer or Moderna vaccines or single-dose J&J vaccine. Querying the billing data for CPT codes generated 1462 procedures for the year. After excluding patients without rhegmatogenous etiology, total of 1047 patients were analyzed.

Various baseline characteristics described in [Table 1](#) were found to be similar between Prior-, Later-, and Never-Vax cohorts; however, there was a significantly ($P = .0487$) lower proportion of Never-Vax patients who presented within 1 day of symptoms onset (6.9%) compared with Prior-Vax patients (10%). Vaccination rate for the group as a whole was below that reported by the Minnesota Department of Health (MDH; [Figure 1, A](#)).¹⁷ When analyzing vaccination rates of the 3 metropolitan regions of our offices, Duluth and St Cloud showed the highest (72%) and lowest (47%), respectively ([Figure 1, B](#)).

Approximately 17.2% of the study population resided outside of Minnesota ([Figure 1, C](#)), with the majority trav-

TABLE 1. Characteristics of Patients Within Different COVID-19 Vaccination Cohorts

	Total (N = 1047)	Prior-Vax (n = 391; 37.3%)	Later-Vax (n = 250; 23.9%)	Never-Vax (n = 406; 38.8%)	P Values
Male gender, %	64.1	60.4	66.4	66.3	.4390
Age, y, mean ± SD	61.4 ± 12.9	64.1 ± 11.6	61.6 ± 13.1	58.7 ± 13.4	.6734
Caucasian race, %	96.4	96.7	96.0	96.3	.8965
Zip code–derived median household income (USD), mean ± SD	78,250.37 ± 24,892.48	79,610.70 ± 25,033.50	78,976.54 ± 25,347.97	76,480.84 ± 24,420.89	.8890
Time to surgical repair, d, mean ± SD	2.0 ± 4.4	1.6 ± 3.2	2.4 ± 5.2	2.3 ± 4.8	.7621
Duration of symptoms, d, median (interquartile range)	7 (3-14)	5 (3-14)	7 (3-21)	7 (3-21)	.6331
Seeking treatment within 1 d of symptom onset, %	8.8	10	9.5*	6.9**	.5987*
Established patients, %	15.7	16.6	16.9	14.5	<i>P</i> = .2398

USD = US dollars.

Characteristics were similar between all 3 vaccination cohorts (Prior-Vax = patients who initially presented for care already vaccinated for COVID-19; Later-Vax = patients who initially presented unvaccinated but subsequently received vaccination during their postoperative course; Never-Vax = patients who initially presented unvaccinated and remained as such throughout their postoperative course); however, significantly ($P = .0487$) fewer Never-Vax patients were observed to present for care within 1 day of onset of symptoms compared to Prior-Vax patients.

* and ** indicate statistical significance.

eling for care from neighboring states with lower vaccination rates (Figure 1, A).¹⁸⁻²¹ When the year was divided into 13-week quarters, there was a significant increase ($P < .0001$) in Never-Vax patients seen in quarters 3 (Q3) and 4 (Q4) compared with earlier (Figure 1, D).

• **SURGICAL PROCEDURES AND REOPERATIONS:** Both Later- and Never-Vax cohorts demonstrated lower and higher rates of SB/PPV (Later-Vax = 58.2%; Never-Vax = 37.9%) and complex RD repair (Later-Vax = 15.2%; Never-Vax = 34.8%) procedures, respectively, compared with the Prior-Vax cohort (SB/PPV = 66.7%; Complex RD repair = 5.9%; Figure 2, A). However, there was no significant difference ($P = .8854$) in rates of PR, primary SB, and primary PPV procedures performed among the 3 cohorts. Later- and Never-Vax cohorts also demonstrated a significantly increased ($P \leq .0112$) proportion of patients presenting with retinal redetachments following initial surgical repair (Later-Vax = 7.4%; Never-Vax = 13.5%) compared with the Prior-Vax cohort (5.9%; Figure 2, B).

• **PRIMARY MACULA-OFF AND PROLIFERATIVE VITREO-RETINOPATHY DISEASES:** Both Later- and Never-Vax cohorts demonstrated significantly higher ($P < .0001$) rates of patients with primary mac-off RRDs (Later-Vax = 54%; Never-Vax = 57.9%) compared with the Prior-Vax cohort (44.5%; Figure 2, C). Furthermore, the presence of primary PVR was found to be significantly greater ($P < .0001$) in both Later- (13.6%) and Never-Vax (17.1%) cohorts compared with the Prior-Vax cohort (4.3%; Figure 2, D).

• **LOST TO FOLLOW-UP:** Postoperative follow-up data were collected for all patients who underwent surgical repair of primary RRD. When examining follow-up duration, approximately 12% of Prior-, 9.1% of Later-, and 19.1% of Never-Vax cohorts did not present for a 3-month or later appointment. Patients who were referred back to their referring provider before the 3-month time point for continued care were eliminated, leaving the remaining patients as those who failed to present for follow-up (lost to follow-up). Analysis reveals that although the Prior- and Later-Vax cohorts demonstrated a similar proportion ($P = .7823$) of patients who were lost to follow-up (Prior-Vax = 2.3%; Later-Vax = 2.2%), there was a significantly larger ($P < .0001$) percentage in the Never-Vax cohort (7.7%; Figure 2, E).

• **ESTABLISHED VS NEW PATIENTS:** A patient was deemed “established” if he or she was examined by our practice within 3 years prior to the diagnosis of a primary RRD. Under these criteria, the 3 vaccination cohorts had similar proportions ($P = .6722$) of established patients (Prior-Vax = 16%; Later-Vax = 15.9%; Never-Vax = 15.1%; Figure 3, A). New patients showed greater proportion of mac-off disease compared with established patients across all cohorts (Figure 3, B). Within new patients, the Later- and Never-Vax cohorts had significantly greater ($P < .0001$) proportion of mac-off RRDs (Later-Vax = 59.9%; Never-Vax = 60%) compared with the Prior-Vax cohort (46%). Established patients did not demonstrate significant differences in mac-off disease among the vaccination cohorts (Prior-Vax = 31.9%; Later-Vax = 32.1%; Never-Vax = 31.5%).

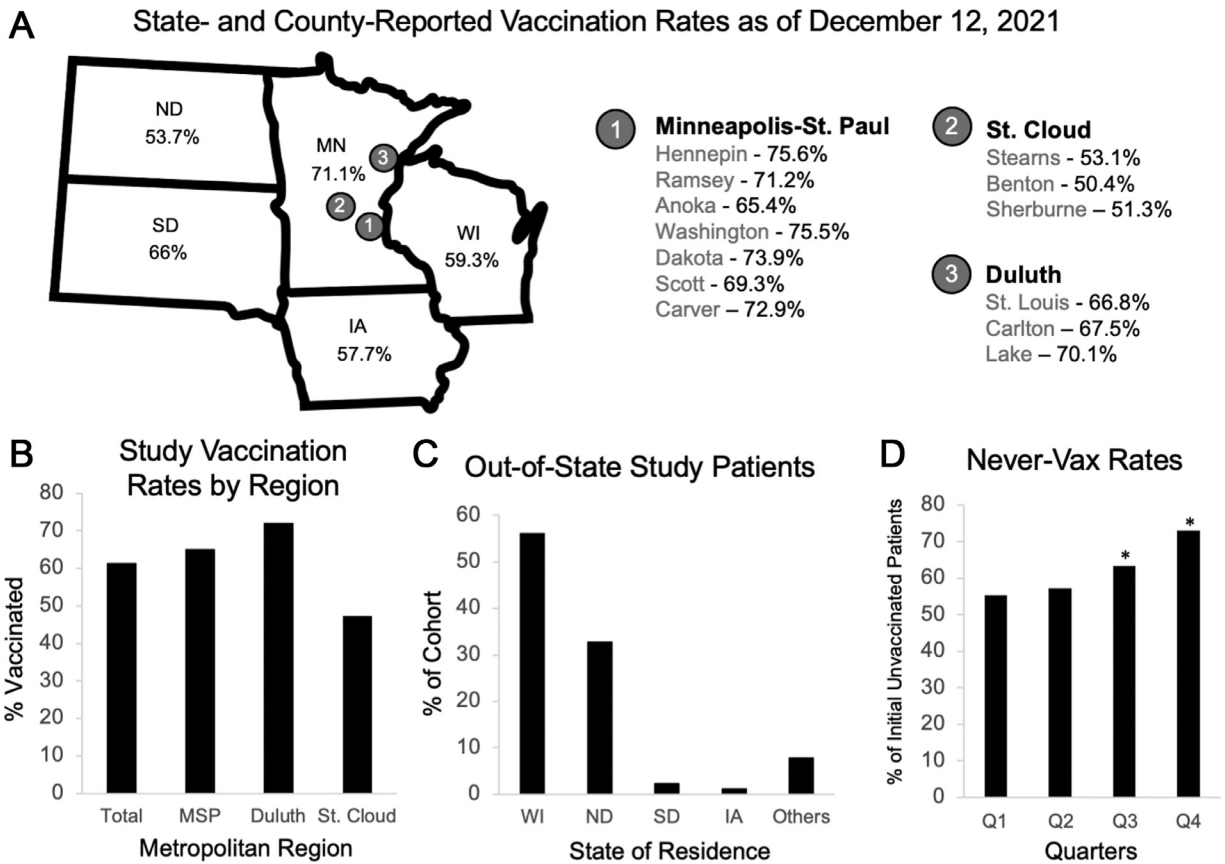


FIGURE 1. Trends in state and county COVID-19 vaccination rates among study population. A (left). Statewide vaccination rates (as defined by individuals receiving at least 1 dose) as reported by the respective state health departments of Minnesota (MN), Wisconsin (WI), North Dakota (ND), South Dakota (SD), and Iowa (IA) as of December 12, 2021. A (right). County-wide vaccination rates are grouped by the 3 metropolitan regions of MN where our offices are located. B. Although the vaccination rate for our study population as a whole (Total) was 61.4%, metropolitan Minneapolis–St Paul (MSP), Duluth, and St Cloud regions were 64.9%, 72%, and 47%, respectively. C. Patients residing outside of MN that were treated by our practice totaled 17.2% (180 patients) of our study population, with the majority coming from WI and ND. D. Analyzing the proportion of patients based on 13-week quarters of the year presenting unvaccinated prior to surgery (initial unvaccinated patients) and remaining unvaccinated throughout their postoperative course (Never-Vax) showed a consistent significant increase ($P < .0001$, indicated by an asterisk) as the year progressed.

• **YOUNGER VS OLDER PATIENTS:** Using age group distributions established by MDH in reporting vaccination rates,¹⁷ we analyzed differences in primary RRD presentation among various ages. The majority of our study population was aged ≥ 50 years (Figure 4, A), and we excluded patients aged < 18 years from analysis because of insufficient sample size (total of 5 patients). There was no significant difference ($P = .5843$) in age of patients seen in our offices among the 3 metropolitan regions (MSP = 62.74 ± 12.85 years; St Cloud = 63.4 ± 12.81 years; Duluth = 64.51 ± 12.25 years [mean \pm SD]; Figure 4).

The proportion of patients belonging to the Prior-Vax cohort was highest in those aged ≥ 65 years (65+; 43.9%) and significantly lower ($P < .0001$) in younger ages (50-64 years = 34.6%; 18-49 years = 25.5%; Figure 4, B). Conversely, the proportion of patients belonging to the Never-Vax cohort was lowest in patients aged ≥ 65 years (30.6%)

and greater in younger age groups (50-64 years = 42.7%; 18-49 years = 51.8%). Vaccination rates remained steady for patients in the Later-Vax cohort across age groups (≥ 65 years = 25.5%; 50-64 years = 22.7%; 18-49 years = 22.6%; $P = .3952$). When analyzing rates of mac-off RRDs by age, younger patients demonstrated significantly lower ($P < .0001$) mac-off rates (50-64 years = 45.6%; 18-49 years = 40.9%) compared to patients aged ≥ 65 years (60.3%; Figure 4, C).

• **TRAVEL DISTANCE:** After excluding 12 traveling patients with addresses > 700 miles from our clinics, geographic analysis showed that patients in the Never-Vax cohort (median = 35 miles) traveled significantly ($P \leq .0002$) farther for care compared with both Later- (median = 25.45 miles) and Prior-Vax (median = 22.3 miles) cohorts (Figure 5, A). There was no significant differ-

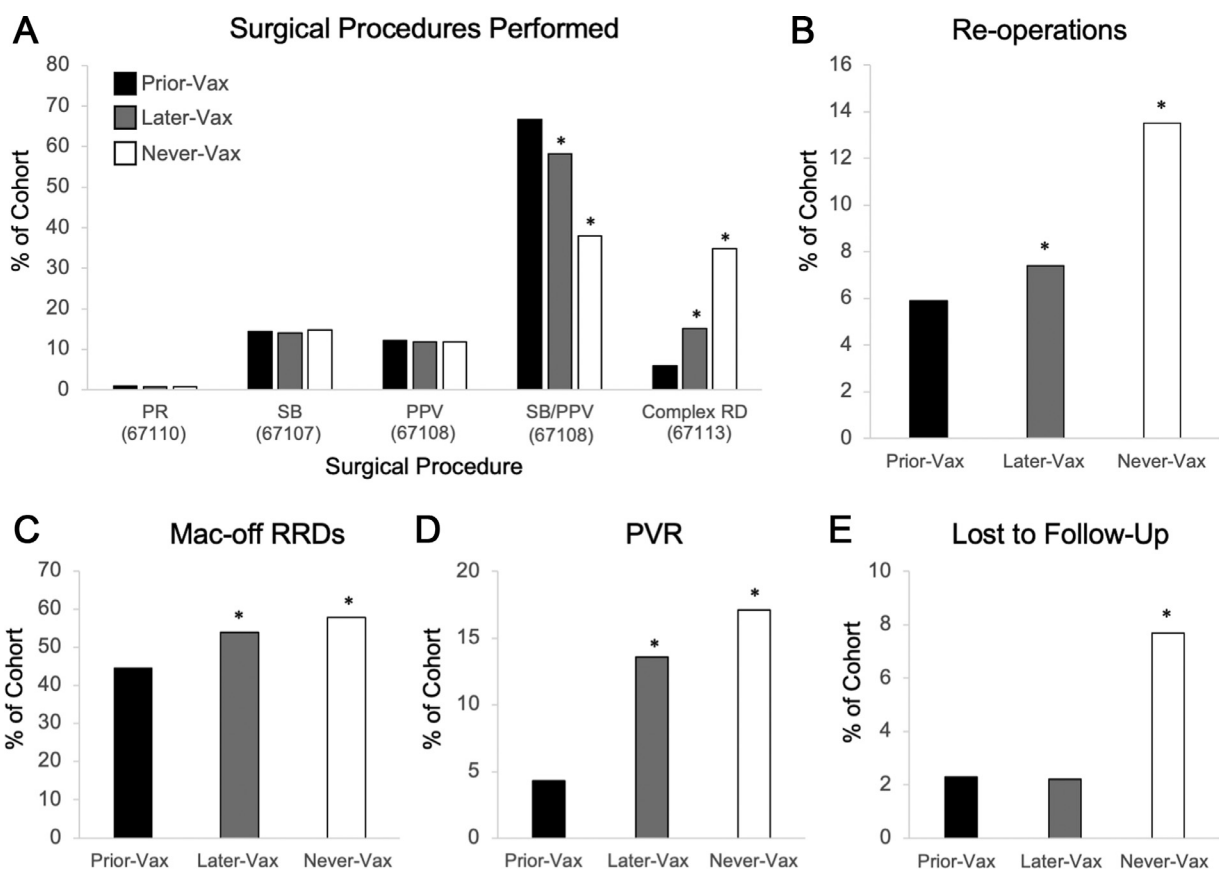


FIGURE 2. Trends in primary rhegmatogenous retinal detachments and surgical repair. Analysis of surgical procedures for repair of primary rhegmatogenous retinal detachments (RRDs) include pneumatic retinopexy (PR; CPT code 67110), primary scleral buckle (SB; 67107), primary pars plana vitrectomy (PPV; 67108), combination of SB and PPV (SB/PPV; 67108), and complex repair of retinal detachment (complex RD; 67113). The Never-Vax cohort demonstrated (A) significant increase in proportion of Complex RD (34.8%, $P < .0001$) and significant decrease in proportion of SB/PPV (37.9%, $P = .0118$) procedures performed compared to the Prior-Vax cohort (SB/PPV = 66.7%, Complex RD = 5.9%). The Later-Vax cohort demonstrated a significant decrease in proportion of SB/PPV (58.2%, $P = .0146$) and a significant increase in proportion of Complex RD (15.2%, $P = .1008$) procedures performed compared to the Prior-Vax cohort. There were no significant differences ($P = .8854$) observed in the proportions of PR, SB, and PPV procedures performed among the 3 cohorts. The proportion of retinal redetachments requiring subsequent surgical intervention was also analyzed and found to be (B) significantly increased for the Later- (7.4%, $P = .0112$) and Never-Vax (13.5%, $P < .0001$) cohorts compared to the Prior-Vax cohort (5.9%). Furthermore, Later- and Never-Vax cohorts presented with significantly increased (C) macula-off (Mac-off) disease (Prior-Vax = 44.5%; Later-Vax = 54%, $P < .0001$; Never-Vax = 57.9%, $P < .0001$) and (D) primary proliferative vitreoretinopathy (PVR) pathology (Prior-Vax = 4.3%; Later-Vax = 13.6%, $P < .0001$; Never-Vax = 17.1%, $P < .0001$) compared to the Prior-Vax cohort. Analysis of patients who were (E) lost to follow-up showed no significant ($P = .7823$) difference between Prior- (2.3%) and Later-Vax (2.2%) cohorts; however, the Never-Vax cohort (7.7%) showed significantly ($P < .0001$) greater proportion of patients. *Statistical significance.

ence ($P = .8335$) in travel distance between mac-on (median = 22 miles) and mac-off patients (median = 24.2 miles), nor was there any significant difference ($P = .1411$) observed among the 3 vaccination cohorts within patients with mac-off RRDs (Prior-Vax = 18.25 miles; Later-Vax = 24.2 miles; Never-Vax = 24.1 miles [median]; Figure 5, B and C).

Furthermore, there was no significant difference ($P = .1390$) between new (median = 23.3 mile) and established (median = 17.3 miles) patients (Figure 5, D). Within new patients, we observed the Never-Vax cohort

traveled significantly farther ($P \leq .0237$) for care (median = 26.5 miles) compared with Prior- (median = 22.1 miles) and Later-Vax (19.7 miles) cohorts (Figure 5, E).

- **VISUAL ACUITY:** The Later- and Never-Vax cohorts presented with significantly worse ($P \leq .0006$) initial and final BCVA compared with the Prior-Vax cohort (Figure 6, A). There were no significant differences ($P = .1422$) in initial and final BCVA between Later- and Never-Vax cohorts. This trend persisted when analyzing patients with mac-off disease (Figure 6, B) and those new to our clinic (Figure 6, C).

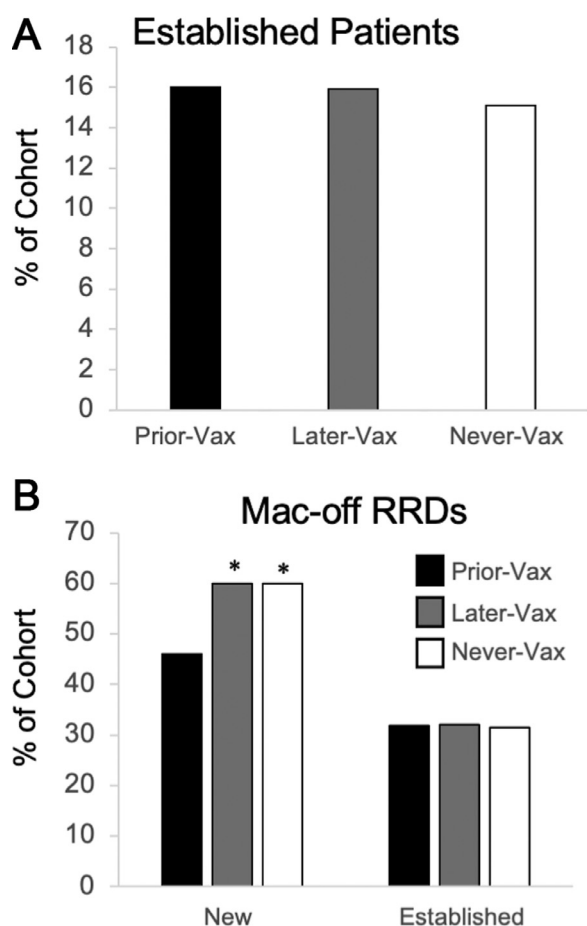


FIGURE 3. Trends in primary rhegmatogenous retinal detachments by new and established patients. Patients were deemed “established” if they were previously seen in our clinic within 3 years of initial RRD diagnosis. **A.** There did not appear to be a significant ($P = .6722$) difference in the number of established patients among the 3 vaccination cohorts (Prior-Vax = 16%; Later-Vax = 15.9%; Never-Vax = 15.1%). **B (left).** When analyzing the proportion of mac-off disease in new and established patients based on vaccination status, new patients who were unvaccinated at the time of initial RRD diagnosis (Later-Vax = 59.9%; Never-Vax = 60%) exhibited significantly ($P < .0001$) greater proportion of mac-off disease compared with Prior-Vax patients (46%). **B (right).** There were no significant differences observed in mac-off disease among the 3 vaccination groups within established patients (Prior-Vax = 31.9%; Later-Vax = 32.1%; Never-Vax = 31.5%; $P = .9115$). *Statistical significance.

DISCUSSION

Multiple factors affect the development of mac-off disease in the setting of primary RRD including pseudophakia, site of retinal break(s), degree of vitreous liquefaction, bullous configuration, axial length, and age.^{1,2} Socioeconomic and demographic statuses are implicated as important risk fac-

tors for decreased surgical success and worse clinical outcomes.²²⁻²⁴ The pandemic has further exacerbated these preexisting factors.⁵⁻⁸

Based on our PubMed/Medline database search, we believe this is the first study to investigate whether COVID-19 vaccine hesitancy has broader implications for clinical trends in emergent ophthalmic conditions. Our findings suggest that patients who are proactive in obtaining vaccination are less likely to suffer significant RRD disease and have better clinical outcomes. This may be facilitated by a higher degree of medical compliance because of decreased pandemic-related fear and anxiety, as suggested by lower rates of hospitalization and death from COVID-19 infection when compared to the unvaccinated.^{25,26}

Even though our clinics are based in major metropolitan regions within Minnesota, we do treat a significant amount of rural and out-of-state patients. Previous studies have shown that rural and lower socioeconomic communities exhibit greater COVID-19 vaccine hesitancy.²⁷⁻³⁰ As such, the vaccination rate for our study population was lower than that reported by MDH. The lowest rate was observed in patients presenting to our St Cloud office, which is reflective of lower vaccination rates locally and from North and South Dakota patients traveling for care to this clinic. Patients presenting to our MSP offices had a lower vaccination rate compared with our Duluth office, likely because of the availability of our MSP offices for emergent after-hours appointments.

Vaccine hesitancy is defined by the WHO as a delay or refusal of immunization when it is available.¹³ We labeled a patient as vaccine hesitant if he or she initially presented unvaccinated and remained so throughout their postoperative course lasting a minimum of 3 months. Because we analyzed clinical trends for a full year after the availability of COVID-19 vaccines, we observed a significant increase in vaccine hesitancy during the latter half of the year.

A likely explanation is that initial vaccine scarcity meant a significant portion of patients presenting unvaccinated earlier in the year had the intention to get the vaccine but lacked access. Once supply became more plentiful, they were able to vaccinate during their postoperative course. As access to vaccines became less of a barrier later in the year, unvaccinated patients were more likely to exhibit vaccine hesitancy because of a variety of reasons such as distrust of the medical field and belief in misinformation.^{28,29}

The presence of primary PVR is a poor prognostic factor associated with delayed presentation.³¹ Primary RRD patients who were initially unvaccinated for COVID-19 demonstrated more advanced retinal pathology such as mac-off status and primary PVR, the highest of which was observed in vaccine-hesitant patients. The result was a greater number of complex surgical interventions and increased retinal redetachments requiring repeat surgeries. Interestingly, this trend was only observed in patients who were new to our clinic, as established patients had similar rates of mac-off disease.

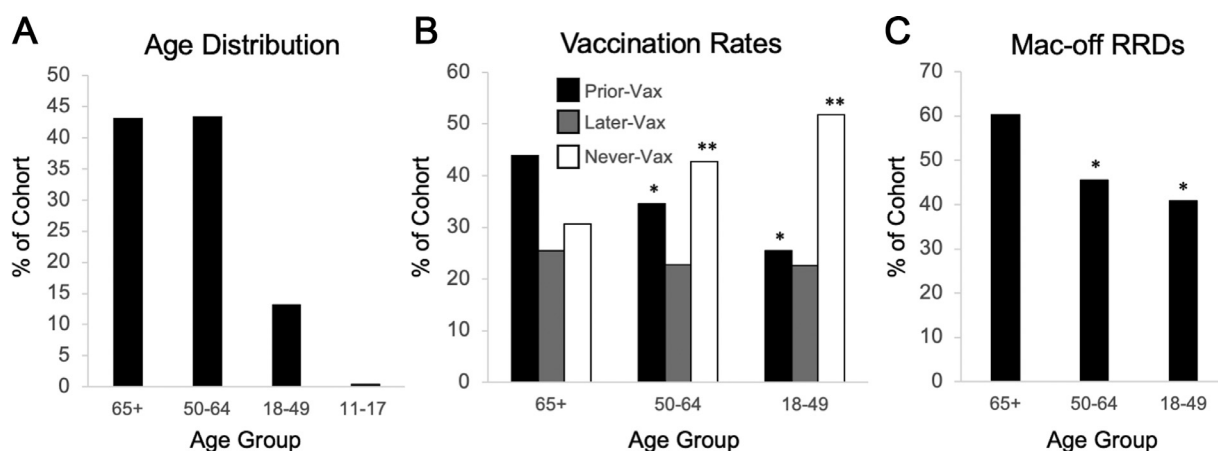


FIGURE 4. Trends in primary rhegmatogenous retinal detachments by age group. **A.** Based on the age groups set by the MN Department of Health for the reporting of COVID-19 vaccination rates, analysis of our study population showed the majority to be 50 years of age or older, with an even distribution between those aged ≥ 65 years and those between ages 50 and 64 years. Since our study population contained only 5 patients aged <18 years (age range 11-17 years), they were excluded from further analysis. There was no significant ($P = .5843$) difference in age of patients seen among the 3 metropolitan regions (MSP = 62.74 ± 12.85 years; St Cloud = 63.4 ± 12.81 years; Duluth = 64.51 ± 12.25 years [mean \pm SD]). **B.** Analysis of vaccination trends among the different age groups revealed that those aged ≥ 65 years are the most likely to be vaccinated at initial diagnosis of primary RRD (Prior-Vax = 43.9%; black bars) and the least likely to remain unvaccinated throughout the study (Never-Vax = 30.6%; white bars). The proportion of patients in the Prior-Vax cohort appeared to significantly ($P < .0001$, indicated by a single asterisk) decline in younger age groups (50-64 years = 34.6%; 18-49 years = 25.5%), whereas the concurrent proportion of patients in the Never-Vax cohort appeared to significantly ($P < .0001$, indicated by double asterisks) increase (50-64 years = 42.7%; 18-49 years = 51.8%). The proportion of patients in the Later-Vax cohort (gray bars) did not appear to differ significantly ($P = .3952$) across age groups (≥ 65 years = 25.5%; 50-64 years = 22.7%; 18-49 years = 22.6%). **C.** When analyzing the proportion of each age cohort presenting with mac-off disease, we found a significantly ($P < .0001$, indicated by a single asterisk) lower proportion in younger age groups (≥ 65 years = 60.3%; 50-64 years = 45.6%; 18-49 years = 40.9%).

Studies have shown that COVID-19 vaccination rates are much lower in younger populations, likely because of lower perceived seriousness of infection by this age group.^{32,33} Data reported by MDH also supports this, where patients in the age categories of ≥ 65 years, 50-64 years, and 18-49 years were vaccinated at a rate of 97%, 79%, and 69%, respectively, by our study end point.¹⁷ We observed highest rates of vaccinated patients in older groups with a subsequent decline in younger groups. Conversely, the proportion of vaccine-hesitant patients appeared to increase in younger groups. We also observed a higher proportion of older patients present with mac-off RRD; however, this is likely related to ocular features of advanced age (ie, presence of a posterior vitreous detachment and increased vitreous liquefaction)^{1,2} instead of a direct effect from vaccines.

It has been well documented that people living in rural areas are less likely to undergo COVID-19 vaccination.^{34,35} We used the distance traveled by patients for care as a surrogate for health care access. We found that patients who traveled the farthest for care tended to be vaccine hesitant, especially those that were new to our clinic. Poorer access to ophthalmic care certainly contributed to more advanced disease among this population. The end result was that vaccinated patients presented with significantly better BCVA

and had improved clinical outcomes compared with those who initially presented unvaccinated.

There were several important limitations to our study. Because of its retrospective nature, there was inherent confirmation bias. Vaccination status after surgery relied on patient self-reporting, but verification by our clinic staff was attempted. It is possible that patients whom we considered vaccine hesitant may have obtained vaccination after the postoperative period with our practice; however, this delay in vaccination still conforms to the definition of vaccine hesitancy by the WHO.¹³ We are unable to further verify vaccination status afterwards as we lack access to their general medical information.

The parameters by which we established the various vaccination cohorts for analysis are artificial and do not reflect nuances in rationale used by individual patients when deciding whether to undergo vaccination. It is conceivable that vaccines could modify an individual's ocular response to an insult such as RRD; however, this was not explicitly investigated. As the majority of our patient population is Caucasian with a median household income higher than national median, this limits the applicability of our results across various racial and socioeconomic groups.

Our geographical area may additionally limit the broader applicability of this study. Furthermore, rates of COVID-19

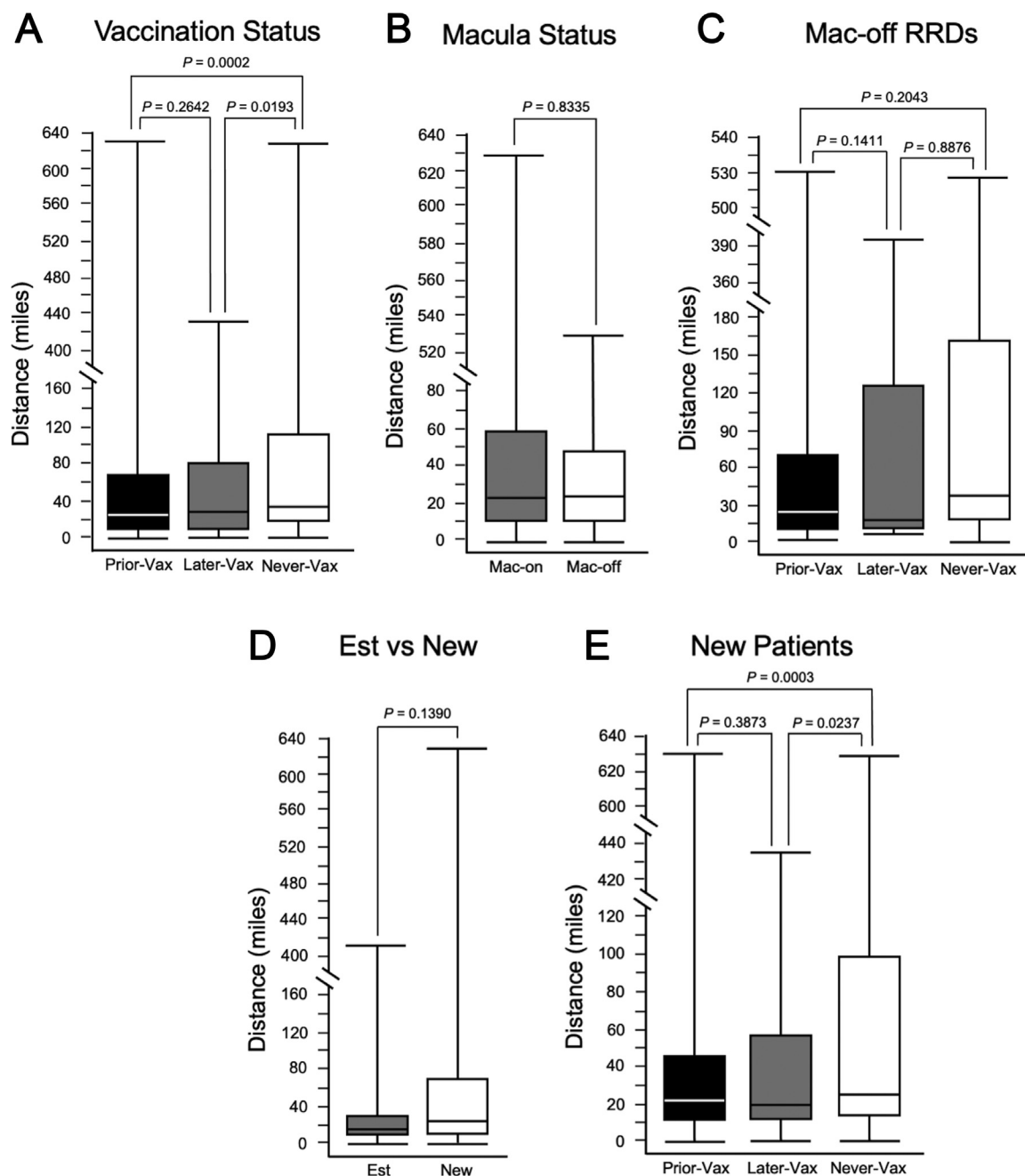


FIGURE 5. Distribution of travel distance by vaccination cohort. Box-and-whisker plot illustrating distribution of distance to clinic (miles) traveled by patients in various cohorts. The box depicts the interquartile range, the line within the box depicts the median, and the line bars above and below the box depict maximum and minimum range, respectively. **A.** No significant ($P = .2642$) differences were observed in median distribution of travel distance between patients in the Prior- (median = 22.3 miles) and Later-Vax cohorts (median = 25.45 miles); however, patients in the Never-Vax cohort (median = 35 miles) traveled significantly greater distances for care compared to Prior- ($P = .0002$) and Later-Vax ($P = .0193$) cohorts. **B.** There was no significant difference in median distribution ($P = .8335$) between patients with mac-off disease (median = 24.2 miles) compared to patients with mac-on disease (median = 22 miles). **C.** Further analysis based on vaccination status of mac-off RRD patients revealed no significant difference ($P = .1411$) in median distribution among Prior- (median = 18.25 miles) and Later-Vax (median = 24.2 miles) cohorts, Prior- and Never-Vax (median = 24.1 miles) cohorts ($P = .2043$), and Later- and Never-Vax cohorts ($P = .8876$). **D.** We also found no significant difference ($P = .1390$) in median distribution between new (median = 23.3 miles) and established patients (median = 17.3 miles). **E.** When further analyzing new patients based on vaccination status, those in the Never-Vax cohort traveled significantly farther (median = 26.5 miles) for care compared to both Later- (median = 19.7 miles; $P = .0237$) and Prior-Vax cohorts (median = 22.1 miles; $P = .0003$); however, there was no significant difference in median distribution between Prior- and Later-Vax cohorts ($P = .3873$).

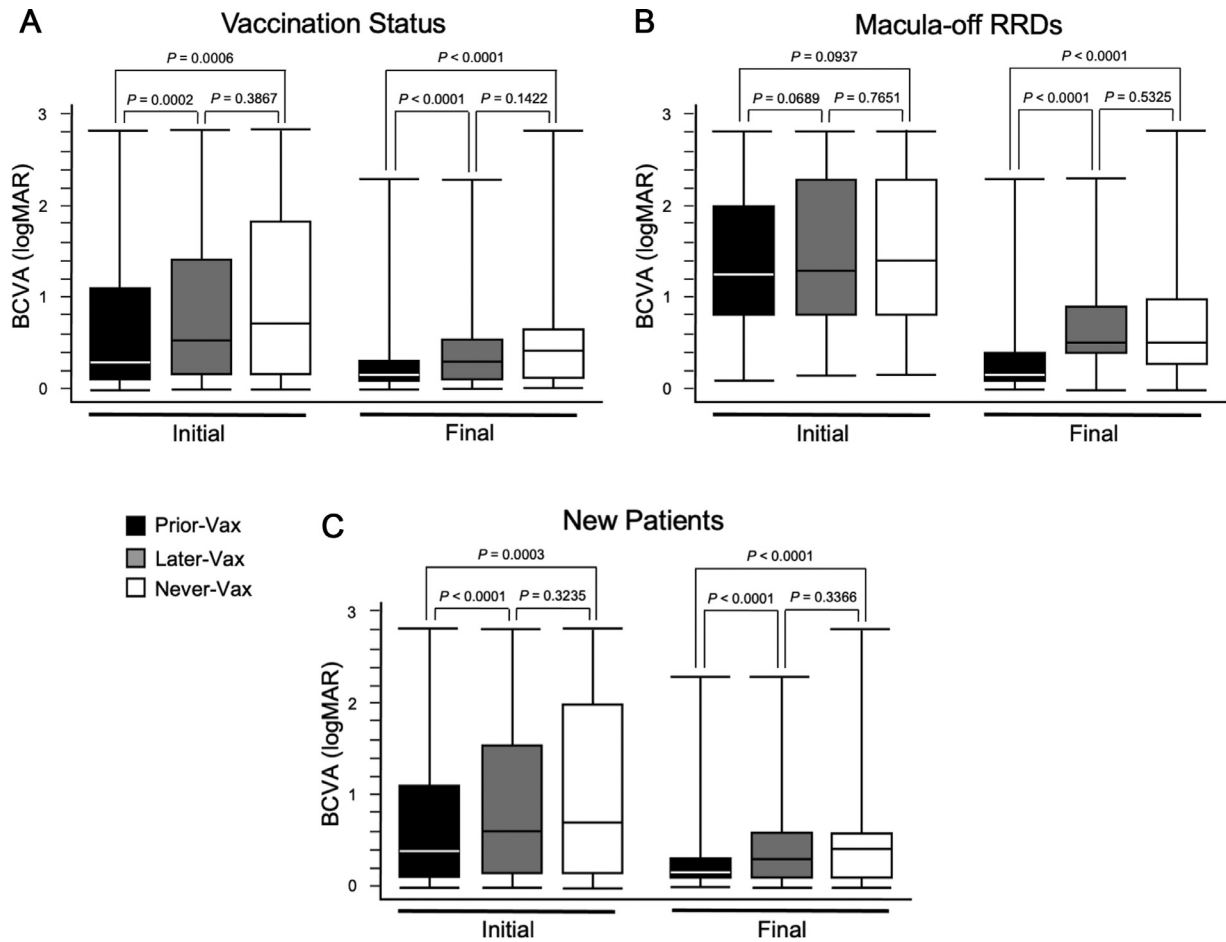


FIGURE 6. Distribution of visual acuity by vaccination cohort. Box-and-whisker plot illustrating distribution of logMAR best-corrected visual acuity (BCVA) among the Prior- (black box), Later- (grey box), and Never-Vax (white box) cohorts from initial and final clinical visits. The box depicts the interquartile range, the line within the box depicts the median, and the bars above and below the box depict maximum and minimum range, respectively. **A.** When considering the vaccination status of all patients presenting with primary RRDs, the Never-Vax cohort showed both significantly worse initial BCVA (median = 0.70 logMAR; Snellen equivalent, 20/100; $P = .0006$) and final BCVA (median = 0.40 logMAR; Snellen equivalent, 20/50; $P < .0001$) compared to the Prior-Vax cohort (Initial: median = 0.30 logMAR; Snellen equivalent, 20/40; Final: median = 0.18 logMAR; Snellen equivalent, 20/30). Although the Later-Vax cohort also showed significantly worse initial BCVA (median = 0.54 logMAR; Snellen equivalent, 20/70; $P = .0002$) and final BCVA (median = 0.30 logMAR; Snellen equivalent, 20/30; $P < .0001$) compared to the Prior-Vax cohort, there was no significant difference when compared to the Never-Vax cohort (Initial: $P = .3867$; Final: $P = .1422$). **B.** When evaluating only patients presenting with mac-off disease, there was no significant difference (Prior- vs Later-Vax: $P = .0689$; Prior- vs Never-Vax: $P = .0937$; Later- vs Never-Vax: $P = .7651$) among the 3 vaccination cohorts with regard to initial BCVA (Prior-Vax: median = 1.24 logMAR; Snellen equivalent, 20/350; Later-Vax: median = 1.30 logMAR; Snellen equivalent, 20/400; Never-Vax: median = 1.40 logMAR; Snellen equivalent, 20/500); however, both Later- and Never-Vax cohorts showed significantly worse ($P < .0001$) final BCVA (Later-Vax: median = 0.54 logMAR; Snellen equivalent, 20/70; Never-Vax: median = 0.54 logMAR; Snellen equivalent, 20/70) compared with the Prior-Vax cohort (median = 0.18 logMAR; Snellen equivalent, 20/30). **C.** When evaluating only patients who were new to our clinic, both Later- and Never-Vax cohorts showed significantly worse (Later-Vax: $P < .0001$; Never-Vax: $P = .0003$) initial BCVA (Later-Vax: median = 0.60 logMAR; Snellen equivalent, 20/80; Never-Vax: median = 0.70 logMAR; Snellen equivalent, 20/100) compared with the Prior-Vax cohort (median = 0.40 logMAR; Snellen equivalent, 20/50); however, there was no significant difference ($P = .3235$) between the Later- and Never-Vax cohorts. Although both Later- and Never-Vax cohorts also showed significantly worse ($P < .0001$) final BCVA (Later-Vax: median = 0.30 logMAR; Snellen equivalent, 20/40; Never-Vax: median = 0.40 logMAR; Snellen equivalent, 20/50) compared with the Prior-Vax cohort (median = 0.18 logMAR; Snellen equivalent, 20/30), there was no significant difference ($P = .3366$) between Later- and Never-Vax cohorts.

vaccinations and degrees of public health measures taken by local governments varied greatly, limiting extrapolation of our data to other regions of the country. Timing of surgery after diagnosis of RRD did not differ between cohorts, indicating vaccination status did not affect patient access to surgery. Variations in RRD presentation due to factors such as seasonal weather patterns and holidays may have influenced our clinical trends reported.

At the conclusion of this study, only 70.2% of the US population has received at least 1 dose of the COVID-19 vaccines.¹² Factors associated with vaccine hesitancy are numerous and may have implications for other ocular diseases such as diabetic retinopathy and glaucoma. We must take these associations into consideration when treating vaccine-hesitant patients as they often present with more advanced disease and suffer worse clinical outcomes.

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