Vaccine 41 (2023) 1649–1656

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Real-world uptake of COVID-19 vaccination among individuals expressing vaccine hesitancy: A registry-linkage study

Kristin L. Andrejko [a,b,1], Jennifer F. Myers [a,1], Nozomi Fukui [a], Lauren Nelson [a], Rui Zhao [a], John Openshaw [a], James P. Watt [a], Seema Jain [a], Joseph A. Lewnard [b,c,d,*], Jake M. Pry [a,e,*], on behalf of the California COVID-19 Case-Control Study Team [2]

[a] California Department of Public Health, Richmond, CA, United States
[b] Division of Epidemiology and Biostatistics, School of Public Health, University of California, Berkeley, CA, United States
[c] Division of Infectious Diseases & Vaccinology, School of Public Health, University of California, Berkeley, CA, United States
[d] Center for Computational Biology, College of Engineering, University of California, Berkeley, CA, United States
[e] Department of Public Health Sciences, School of Medicine, University of California, Davis, CA, United States

ARTICLE INFO

Article history:
Received 24 August 2022
Received in revised form 9 January 2023
Accepted 27 January 2023
Available online 1 February 2023

Keywords:
Covid-19
Flu
Influenza
Vaccine
Self-report
Vaccine hesitancy
Vaccine registry
SARS-COV-2

ABSTRACT

Introduction: Uptake of COVID-19 vaccination remains suboptimal in the United States and other settings. Though early reports indicated that a strong majority of people were interested in receiving the COVID-19 vaccine, the association between vaccine intention and uptake is not yet fully understood. Our objective was to describe predictors of vaccine uptake, and estimate the sensitivity, specificity, and predictive values of self-reported COVID-19 vaccine status compared to a comprehensive statewide COVID-19 vaccine registry.

Methods: A cohort of California residents that received a molecular test for SARS-CoV-2 infection during 24 February-5 December 2021 were enrolled in a telephone-administered survey. Survey participants were matched with records in a statewide immunization registry. Cox proportional hazards model were used to compare time to vaccination among those unvaccinated at survey enrollment by self-reported COVID-19 vaccination intention.

Results: Among 864 participants who were unvaccinated at the time of interview, 272 (31%) had documentation of receipt of COVID-19 vaccination at a later date; including 194/423 (45.9%) who had initially reported being willing to receive vaccination, 41/185 (22.2%) who reported being unsure about vaccination, and 37/278 (13.3%) who reported unwillingness to receive vaccination. Adjusted hazard ratios (aHRs) for registry-confirmed COVID-19 vaccination were 0.49 (95% confidence interval: 0.32–0.76) and 0.21 (0.12–0.36) for participants expressing uncertainty and unwillingness to receive vaccination, respectively, as compared with participants who reported being willing to receive vaccination. Time to vaccination was shorter among participants from higher-income households (aHR = 3.30 [2.02–5.39]) and who reported co-morbidities or immunocompromising conditions (aHR = 1.54 [1.01–2.36]). Sensitivity of self-reported COVID-19 vaccination status was 82% (80–85%) overall, and 98% (97–99%) among those referencing vaccination records; specificity was 87% (86–89%).

Conclusion: Willingness to receive COVID-19 vaccination was an imperfect predictor of real-world vaccine uptake. Improved messaging about COVID-19 vaccination regardless of previous SARS-CoV-2 infection status may help improve uptake.

© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

* Corresponding authors at: 2121 Berkeley Way, Berkeley, CA 94720, United States (J.A. Lewnard). 850 Marina Bay Parkway, Richmond, CA 94804, United States (J.M. Pry).
E-mail addresses: jlewnard@berkeley.edu (J.A. Lewnard), jmpry@ucdavis.edu (J.M. Pry).

[1] KLA and JFM contributed equally to the study.

[2] Members of the California COVID-19 Case-Control Study Team include: Helia Samani, Nikolina Walas, Erin Xavier, Diana J. Poindexter, Najla Dabbagh, Michelle M. Spinosa, Shrey Saretha, Adrian F. Cornejo, Hyemin Park, Christine Wan, Miriam I. Bermejo, Amanda Lam, Amandeep Kaur, Ashly Dyke, Diana Felipe, Maya Spencer, Savannah Corredor, Yasmine Abdulrahim, Camilla M. Barbaduomo, Zheng N. Dong, Anna T. Fang, Paulina M. Frost, Timothy Ho, Mahsa H. Javadi, Sophia S. Li, Vivian H. Tran, Jennifer L. DeGuzman, and Christine Wan.

https://doi.org/10.1016/j.vaccine.2023.01.066
0264-410X/© 2023 The Authors. Published by Elsevier Ltd.
This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Background

Suboptimal uptake of COVID-19 vaccination among eligible individuals in the United States (US) and other settings has contributed to preventable COVID-19 cases, hospitalizations, and deaths [1]. Addressing barriers to timely vaccination against COVID-19 is thus a priority to mitigate disease burden. While surveys have provided an important tool for assessing vaccine hesitancy and acceptance across differing communities, alignment between participants' self-reported vaccine intentions and real-world receipt of vaccination is not well understood [2,3]. Understanding barriers and facilitators of COVID-19 vaccine receipt among individuals who express hesitancy, or that preclude vaccine access among individuals who express willingness, could support efforts to maximize vaccine uptake.

The State of California first made COVID-19 vaccines available to health care workers in November 2020; by April 19, 2021, eligibility for COVID-19 vaccination expanded to all California residents aged 16 years and older [4,5]. Healthcare providers administering COVID-19 vaccines in California are required to report all doses administered to local or state-level public health authorities, enabling comprehensive tracking of vaccine uptake within the state's population via the state-wide immunization registry As of December 5, 2021, 28.5 million (73%) of California's 39.2 million residents were recorded as having received $\geq$ 1 doses of any COVID-19 vaccine within the state [6].

The California Department of Public Health (CDPH) collected data on willingness to receive COVID-19 vaccines among participants enrolled in a test-negative design case-control study throughout COVID-19 vaccine rollout [4,7,8]. To understand the relationship between participants' self-reported vaccine intentions and real-world vaccine uptake, we cross-referenced data from study participants and the state-wide immunization registry to compare COVID-19 vaccine receipt among individuals who expressed hesitancy or willingness to be vaccinated. To further inform uses of self-reported vaccination in research studies, we assessed the accuracy of participants' self-reported COVID-19 vaccination status in comparison with registry-based documentation of COVID-19 vaccination.

2. Methods

2.1. Study population

This analysis used data from participants enrolled between 24 February 2021 and 5 December 2021 in the California COVID-19 Case-Control study, which was undertaken to evaluate risk factors for SARS-CoV-2 infection within the state. Survey methodology has been described elsewhere [4,7,8]. In brief, each day throughout the study period randomly selected California residents who tested positive and negative for SARS-CoV-2 infection were asked to participate in a telephone interview whereby trained interviews administered a structured questionnaire in English and Spanish recording self-reported COVID-19 vaccination status.

2.2. Record linkage with the state-wide immunization registry

The state of California intends to capture all COVID-19 vaccinations occurring within the state to monitor trends, identify gaps in coverage, and inform public health efforts (Fig. 1). We linked participant records across the study and California immunization registry using a previously-described probabilistic framework [9]. We first identified records of vaccine doses administered among all study participants by searching for exact or deterministic matches on zip code of residence and date of birth, and fuzzy matches on first and last name (standardizing text fields by removing uppercase letters, spaces, and special characters). Participants were considered to have no documented receipt of COVID-19 vaccine doses if the best probable match (range: 0.0000–1.0000) in the vaccine registry was < 0.5000 while those with probable match score $\geq$ 0.9525 were considered to have a documented vaccine dose. We undertook manual review of records when one participant was matched to multiple registry vaccine records and/or when match assignment probabilities valued between 0.5000 and 0.9525.

2.3. Inclusion and exclusion criteria

The time-to-vaccination analysis was restricted to participants enrolled from 19 April 2021 onward. Eligibility to receive vaccination was defined by age, per date of the United States Health and Human Services recommendation for a particular age group to receive SARS-CoV-2 vaccination. Participants aged 5–64 years who indicated they had not yet received any doses of a COVID-19 vaccine at the time of enrollment were eligible for inclusion in this sub-study, including primary analysis of factors predicting vaccine receipt (Fig. 1). Participants aged 0–4 years were excluded from this analysis due to their ineligibility for COVID-19 vaccination throughout the study period; individuals aged $\geq$ 65 years were excluded because differing dates of vaccine eligibility for residents of long-term care facilities or other adults aged $\geq$ 65 years precluded reliable measurement of the time from when individuals became eligible for COVID-19 vaccines to when they received an initial dose. We further excluded participants who self-reported medical contraindications for receiving COVID-19 vaccines.

2.4. Statistical analysis

Our primary outcome of interest was the time from age-eligibility of SARS-CoV-2 vaccination to SARS-CoV-2 vaccine initiation as recorded in the immunization registry or censoring if no COVID-19 vaccine doses were received. Participants aged $\geq$ 16 years, $\geq$11 years, or $\geq$ 5 years were considered age-eligible for COVID-19 vaccination on April 19, May 10, and October 29, 2021, respectively [5]. Participants who were vaccinated prior to the date of eligibility (n = 11) were assigned an observation time of 1 day.

We used Cox proportional hazards models to estimate adjusted hazard ratios (aHR) of vaccine uptake throughout the study period. The primary exposure of interest was self-reported intention to receive COVID-19 vaccination. Models adjusted for age, race/ethnicity, sex, annual household income, region of residence within California (**Table S1**), SARS-CoV-2 test result status at the time of enrollment in the study, self-reported comorbid conditions, and self-reported uptake of/adherence to public health mitigation measures including use of face masks and physical distancing, and self-reported anxiety about COVID-19. To account for differences in the study population who remained unvaccinated throughout the study period, participants were compared within regression strata defined by the calendar month of participation in the study. We verified the proportional hazards assumption by testing for slopes in Schoenfeld residuals [10].We then repeated these analyses in subgroups of participants according to their stated intentions (willing, unsure, unwilling) of receiving COVID-19 vaccination. As secondary analyses, we assessed differences in time to initiate COVID-19 vaccination according to participants' stated reasons for vaccine refusal or hesitancy using Cox proportional hazards models, restricted to participants who stated they were unsure or unwilling to receive vaccination.

We also sought to validate participants' self-reported vaccination status using the immunization registry. Participants were each

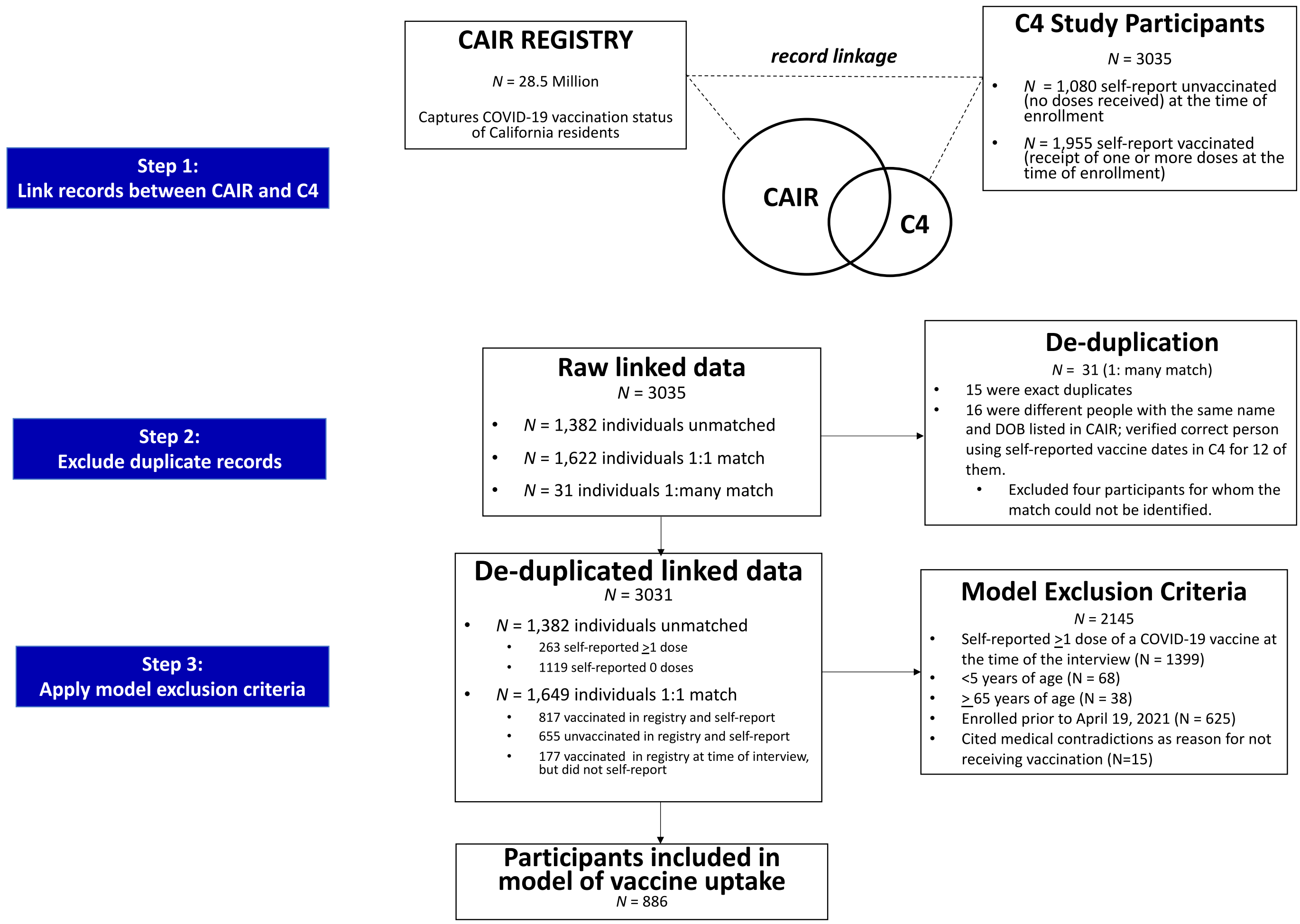

Fig. 1. Flow chart of participants included in CAIR[1], C4 data, and ultimately the analytic data set, Abbreviations **CAIR:** California Immunization Registry; **C4** California COVID-19 Case Control Study, [1]Healthcare providers in 49 of 58 California counties (collectively accounting for 87% of California's population) submit data on vaccine administration directly to the state-wide immunization registry on all COVID-19 vaccine doses administered. In the remaining nine counties, data are linked to the state-wide immunization registry from local-level registries. The San Diego Immunization Registry (SDIR) collects data from providers in San Diego County, while the Healthy Futures (HF) Immunization Registry collects data from providers in the remaining eight counties (Alpine, Amador, Calaveras, Mariposa, Merced, San Joaquin, Stanislaus, and Tuolumne); the state-wide immunization registry receives data from these regional IISs rather than by direct notification from healthcare providers. Reports on greater than 90% of doses administered within the state of California are received by the state-wide immunization registry within one day of the vaccine administration date. However, some vaccination dose submissions may be less timely, such as those from mass vaccination clinics or those that are manually entered into the state-wide immunization registry. N = 3031 individuals were included in the estimates of sensitivity, specificity, positive predictive value, and negative predictive value (Table 3). N = 886 participants are included in the analyses (cox proportional hazard model) assessing the association between stated vaccine acceptance and subsequent vaccine uptake.

categorized into four mutually exclusive categories according to alignment of their self-reported vaccination status and linked data from the immunization registry: self-reported vaccinated with match in immunization registry (A), self-reported vaccinated without match in immunization registry (B), self-reported unvaccinated and match in immunization registry (C), or self-reported unvaccinated and without immunization registry match (D). Vaccination status in the immunization registry was recoded to match the vaccination status of a participant at the time of their telephone interview. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of self-reported vaccination status as compared with registry-documented vaccination status (treated as the "gold standard") were calculated with accompanying 95% confidence intervals via bootstrap resampling. We stratified these calculations by use of a recall aid at the time of study participation, SARS-CoV-2 test result, enrollment period in the study, age, and region. Participants of all ages were included in these analyses. As a sensitivity analysis, we conducted a quantitative bias analysis to assess the extent to which vaccine effectiveness estimates derived from self-reported vaccination status in epidemiologic data sets may be biased due to differential sensitivity and specificity between cases and controls.

All analyses were performed using R (version 3.6.1; R Foundation for Statistical Computing).

2.5. Ethics

The study protocol was approved by the State of California, Health and Human Services Agency, Committee for the Protection of Human Subjects (Project Number: 2021–034).

3. Results

Among 3,035 individuals enrolled between 24 February 2021 – 5 December 2021 and who self-reported their COVID-19 vaccination status, 54% (1622/3035) matched with a single record in the immunization registry, 45.5% (1382/3035) did not have a record of COVID-19 vaccination, and 1% (31/3035) individuals matched with multiple records (Fig. 1). Upon de-duplication of the 31 records with a one-to-many match in the state-wide immunization registry, four records were excluded due to the inability to identify a correct match. Ultimately, 3031 participants were included in the assessment of accuracy of self-reported COVID-19 vaccination status, among whom 35.6% (1080) self-reported having already received $\geq$ 1 dose of COVID-19 vaccine at time of study enrollment (**Table S2**).

For the primary analysis we included a total of 886 individuals who met the inclusion criteria outlined above (Fig. 1**;** Table 1). We found 423 (47.7%) were willing to, 185 (20.8%) were unsure, and 278 (31.3%) were unwilling to receive COVID-19 vaccination (Table 2**; Table S3;** Fig. 2**; Fig. S1**). Among individuals who were unwilling, unsure, or willing to receive COVID-19 vaccination, 13% (37/278), 22% (41/185), 46% (194/423), respectively, matched with a vaccine record as of 5 December 2021.

Adjusted hazard ratio estimates indicated longer time to COVID-19 vaccine uptake among participants who stated they were unsure (aHR: 0.49 [95% CI: 0.32–0.76]) or unwilling (aHR: 0.21 [0.12–0.36]) to initiate COVID-19 vaccination, as compared with participants expressing willingness to be vaccinated (Table 2**; Fig. S2**). The adjusted hazard ratio of vaccine uptake comparing female with male participants was 1.56 (95% CI: 1.12–2.17). Children aged 5–12 (aHR: 2.37 [1.30–4.33]) and teenagers 13–17 (aHR: 2.09 [1.13–3.88]) experienced shorter time to receive vaccination than young adults aged 18–29. Participants from households with an annual income greater than $150,000 had 3.30 (2.02–5.39) times higher adjusted hazards of receiving a COVID-19 vaccine than participants from households with annual income under $50,000. Case participants (SARS-CoV-2 test positive) experienced longer time to vaccinate (aHR: 0.60 [0.43–0.84]) than control participants (SARS-CoV-2 test negative). Time to vaccination was shorter among participants reporting co-morbidities or immunocompromising conditions as compared to (aHR: 1.54 [1.01–2.36]) those without health conditions.

Among the subgroup of participants who stated they were unwilling or unsure about receiving COVID-19 vaccination, younger participants aged 5–12 years (aHR = 14.19 [2.15–93.33]) and 13–17 years (aHR = 3.98 [1.22–12.94]) experienced shorter time to vaccinate compared with participants aged 18–29 years (**Table S4**). Within the subgroup of participants who indicated they were willing to receive COVID-19 vaccination, there were not significant differences in the time to vaccine uptake by age, although point estimates suggested higher uptake among children aged under 18 years (aHR = 1.74 and 1.70 for those aged 5–12 years and 13–17 years, respectively, as compared with 18–29 years). The adjusted hazard ratio of subsequent vaccination among higher income (>$150,000) households as compared with lower income (< $50,000) households among the unwilling or unsure and willing were 5.53 (1.85–16.57) and 2.69 (1.47–4.93), respectively. Time to vaccine uptake was longer among participants who had recently tested positive for SARS-CoV-2 (aHR = 0.23 [0.11–0.47]) if they indicated they were unwilling or hesitant to initiate COVID-19 vaccination; however, this effect was not apparent among the SARS-CoV-2 positive participants who indicated willingness to initiate vaccination (aHR = 0.92 [0.60–1.40]).

Leading reasons for reporting as unsure or unwilling to receive vaccine were concerns about COVID-19 vaccine safety and/or side effects (43%; 199/653), wanted to wait for more research or learn more about COVID-19 vaccines (36%; 165/463), and/or had ideological reasons (21%; 98/463) associated with adjusted hazard ratio estimates of subsequent vaccination 0.91 (0.48, 1.70), 1.10 (0.58, 2.11), and 0.69 (0.24–2.01), respectively (**Table S5**). Time to vaccine uptake was longer among participants who indicated that COVID-19 vaccination should be their personal choice (16%, 76/463) as compared to participants who did not cite this reason (aHR: 0.62 [0.18–2.07]), although this association was not statistically significant. None of the eight participants who cited religious objections as a reason to be unsure or unwilling to receive vaccine subsequently received vaccination as of 5 December 2021.

Table 1
Descriptive attributes of participants included in CAIR and C4 data.

	California COVID-19 Case Control Study (C4) *N* = 886 *N* (%)	**California Immunization Registry (CAIR)** *N* = 30,337,066 *N* (%)
Age		
5–6	30 (3.4)	298,260 (1.0)
7–12	91 (10.3)	1,321,700 (4.4)
13–17	60 (6.8)	1,881,725 (6.2)
18–29	289 (32.6)	5,224,403 (17.2)
30–49	326 (36.8)	9,056,852 (29.9)
50–64	90 (10.2)	6,690,380 (22.1)
Region[1]		
Predominantly Urban Regions		
San Francisco Bay Area	72 (8.1)	6,992,851 (23.1)
Greater Los Angeles Area	106 (12.0)	13,968,657 (46.0)
Greater Sacramento Area	117 (13.2)	1,105,555 (3.6)
San Diego and southern border	116 (13.1)	3,288,437 (10.8)
Predominantly Rural Regions		
Central Coast	85 (9.6)	873,117 (2.9)
Northern Sacramento Valley	97 (10.9)	455,923 (1.5)
San Joaquin Valley	114 (12.9)	2,695,127 (8.9)
Northwestern California	85 (9.6)	337,255 (1.1)
Sierras Region	94 (10.6)	620,144 (2.0)
Race/ ethnicity		
Non-Hispanic White	333 (37.6)	10,135,480 (33.4)
Non-Hispanic Black	64 (7.2)	1,289,690 (4.3)
Hispanic (any race)	272 (30.7)	9,475,691 (31.2)
Asian	54 (6.1)	4,884,233 (16.1)
Native American	16 (1.8)	103,491 (0.3)
Native Hawaiian	3 (0.3)	144,758 (0.5)
Other race	6 (0.7)	2,400,097 (7.9)
More than 1 race	107 (12.1)	625,826 (2.1)
Missing	31 (3.5)	1,277,800 (4.2)
Annual household income		
<$50,000	256 (28.9)	–
$50,000-$100,000	202 (22.8)	–
$100,000-$150,000	88 (9.9)	–
>$150,000	73 (8.2)	–
Refuse/ missing	267 (30.1)	–
Sex		
Male	429 (48.4)	–
Female	457 (51.6)	–
Co-morbid conditions		
No co-morbidities	740 (83.5)	–
Co-morbidities	139 (15.7)	–
Missing	7 (0.8)	–
Anxiety about covid		
Low anxiety	619 (69.9)	–
High anxiety	261 (29.5)	–
Missing	6 (0.7)	–
SARS-CoV-2 Test Result		
Negative	295 (33.3)	–
Positive	591 (66.7)	–
Agreement with social distancing recommendations		
Disagree	61 (6.9)	–
Neutral	130 (14.7)	–
Agree	673 (76.0)	–
Missing	22 (2.5)	–
Agreement with face mask policies		
Disagree	92 (10.4)	–
Neutral	145 (16.4)	–
Agree	629 (71.0)	–
Missing	20 (2.3)	–

Abbreviations: C4 = California COVID-19 Case Control study; CAIR = California Immunization Registry.
[1] We list counties grouped into each region in **Table S1**.

Table 2
Predictors of time to vaccine uptake among participants (*N* = 886) who self-reported that they had not yet received any doses of a SARS-CoV-2 vaccine at the time of the C4 interview.

Participant characteristic	**All participants**		
	Proportion vaccinated	HR (95% CI)	
	Number vaccinated/Total (%)	Unadjusted	Adjusted
Vaccine willingness during C4 interview			
Willing to get the COVID-19 vaccine	194/423 (45.9)	ref.	ref.
Unsure about the COVID-19 vaccine	41/185 (22.2)	0.40 (0.29, 0.56)	0.49 (0.32, 0.76)
Unwilling to get the COVID-19 vaccine	37/278 (13.3)	0.23 (0.16,0.33)	0.21 (0.12, 0.36)
Age of participant			
5–12	38/121 (31.4)	5.24 (3.40, 8.09)	2.37 (1.30, 4.33)
13–17	19/60 (31.7)	1.30 (0.79, 2.14)	2.09 (1.13, 3.88)
18–29	97/289 (33.6)	ref.	ref.
30–49	95/326 (29.1)	0.87 (0.55, 1.16)	0.96 (0.65, 1.41)
50–64	23/90 (25.6)	0.74 (0.47, 1.18)	0.71 (0.35, 1.44)
Region[1]			
San Francisco Bay Area	36/72 (50.0)	ref.	ref.
Greater Los Angeles Area	34/106 (32.1)	0.49 (0.31, 0.79)	0.71 (0.38, 1.34)
Greater Sacramento Area	36/117 (30.8)	0.52 (0.33, 0.83)	0.68 (0.37, 1.26)
San Diego and southern border	39/116 (33.6)	0.66 (0.42, 1.05)	1.09 (0.59, 2.02)
Central Coast	24/85 (28.2)	0.38 (0.22, 0.65)	0.51 (0.26, 1.04)
Northern Sacramento Valley	26/97 (26.8)	0.40 (0.24, 0.67)	0.81 (0.38, 1.71)
San Joaquin Valley	32/114 (28.1)	0.51 (0.32, 0.82)	0.62 (0.32, 1.17)
Northwestern California	19/85 (22.4)	0.37 (0.21, 0.64)	0.70 (0.34, 1.45)
Sierras Region	26/94 (27.7)	0.43 (0.26, 0.72)	0.85 (0.40, 1.80)
Annual household income			
<$50,000	66/256 (25.8)	ref.	ref.
$50,000-$100,000	57/202 (28.2)	1.07 (0.75, 1.54)	1.71 (1.14, 2.55)
$100,000-$150,000	31/88 (35.2)	1.52 (0.99, 2.33)	1.76 (1.06, 2.91)
>$150,000	36/73 (49.3)	2.22 (1.46, 3.37)	3.30 (2.02, 5.39)
Race/ethnicity			
Non-Hispanic white	97/339 (23.4)	ref.	ref.
Asian	31/54 (57.4)	2.79 (1.86, 4.20)	1.67 (0.91, 3.08)
Black	15/64 (23.4)	0.73 (0.42, 1.25)	1.24 (0.53, 2.88)
Hispanic	92/272 (33.8)	1.19 (0.90, 1.59)	1.50 (0.98, 2.28)
More than 1 race	28/107 (26.2)	0.96 (0.63, 1.46)	0.96 (0.54, 1.71)
Other	5/19 (26.3)	0.91 (0.33, 2.49)	0.76 (0.21, 2.67)
Sex			
Male	116/429 (27.0)	ref.	ref.
Female	156/457 (34.1)	1.28 (1.01, 1.63)	1.56 (1.12, 2.17)
Co-morbid conditions			
No co-morbidities	227/740 (30.7)	ref.	ref.
Co-morbidities	43/139 (30.9)	0.93 (0.67, 1.28)	1.54 (1.01, 2.36)
Anxiety about covid			
Low anxiety	176/ 619 (28.4)	ref.	ref.
High anxiety	93/261 (35.6)	1.37 (1.07, 1.76)	1.05 (0.75, 1.49)
SARS-CoV-2 Test Result			
Negative	103/295 (34.9)	ref.	ref.
Positive	169/591 (28.6)	0.68 (0.53, 0.87)	0.60 (0.43, 0.84)
Agreement with social distancing recommendations			
Disagree	9/61 (14.8)	ref.	ref.
Neutral	22/130 (16.9)	1.33 (0.63, 2.80)	1.50 (0.40, 5.69)
Agree	232/673 (34.5)	2.52 (1.34, 4.76)	2.31 (0.66, 8.15)
Agreement with face mask policies			
Disagree	12/92 (13.0)	ref.	ref.
Neutral	33/145 (22.8)	2.10 (1.10, 3.98)	1.16 (0.43, 3.12)
Agree	219/629 (34.8)	3.06 (1.75, 5.37)	1.04 (0.41, 2.65)

Abbreviations: C4 = California COVID-19 Case Control study; ref = reference category; HR = Hazard Ratio.
[1] We list counties grouped into each region in **Table S1**. In a sensitivity analysis, we grouped regions by "predominantly urban" and "predominantly rural" instead of multi-county regions and estimated an unadjusted HR of 1.50 (95% CI: 1.18, 1.91) and adjusted hazards ratio of 1.28 (95% CI 0.93 – 1.78) comparing urban vs. rural counties.

The sensitivity and specificity of self-reporting receipt of one or more doses of COVID-19 vaccine was 82% (95% CI: 80–85%) and 87% (86–89%), respectively, in comparison to vaccine doses recorded in the immunization registry at the time of the telephone interview (**Table S6; Table 3**). The positive predictive value (PPV) and negative predictive value (NPV) of participant-reported vaccination status were 76% (73–78%) and 91% (90–92%), respectively. Sensitivity of self-reported vaccination status was significantly higher among participants who referenced a recall aid; sensitivity was 98% (97–99%) among participants who referenced their vaccination card, 92% (86–96%) among participants who referenced another recall aid (e.g., e-mail, text message, calendar reminder, and/or diary entry for their vaccine appointment), and 45% (38–52%) among participants who did not reference a recall aid. Sensitivity (86% [82–90%] vs. 80% [77–83%]) and specificity (94% [92–95%] vs. 78% [75–81%]) of self-reported vaccination status was significantly higher among cases compared with controls. In a quantitative bias analysis, differential misclassification of self-reported vaccination status by SARS-CoV-2 test result resulted in non-significant overestimates of COVID-19 vaccine effectiveness (**Table S7**). No differences in sensitivity and specificity were apparent within strata of SARS-CoV-2 test result and use of a recall aid;

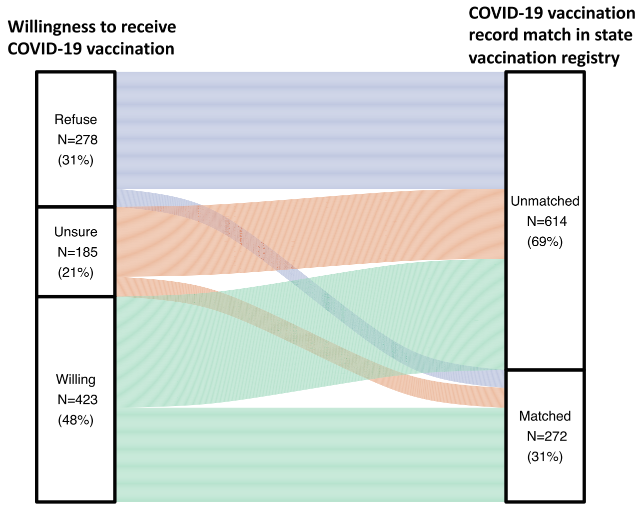

Fig. 2. Stated vaccine acceptance and subsequent vaccine uptake among study participants.

thus, accounting for use of a recall aid results in non-differential misclassification of vaccination status, resulting in underestimates of vaccine effectiveness. Sensitivity analyses estimated agreement between self-reported COVID-19 vaccine manufacturer and dates of initiating COVID-19 vaccination upon comparison of self-report and registry-based documentation (**Table S8**; **Table S9**).

4. Discussion

Among individuals who were unvaccinated at the time of receiving a test for SARS-CoV-2 infection during the period of widespread COVID-19 vaccine availability, we found that COVID-19 vaccination intentions were strongly but imperfectly associated with subsequent initiation of COVID-19 vaccine series. By 5 December 2021, 22% of participants who responded as unsure about receiving COVID-19 vaccines and 13% who expressed unwillingness to receiving COVID-19 vaccines had received at least one dose of COVID-19 vaccine per immunization registry; whereas no record of vaccination was available for 54% of participants who expressed willingness to receive COVID-19 vaccines. Vaccine uptake was fastest among the highest-income households and participants who expressed willingness to receive COVID-19 vaccination. We identified that a positive SARS-CoV-2 test result predicted lower hazard of COVID-19 vaccination, most strikingly, among individuals who reported being unsure about or unwilling to received vaccine. This suggests that there might be opportunities for outreach to encourage vaccine uptake among individuals who have received a positive COVID-19 test result. Additionally, we identified faster time to vaccinate among children as compared to adults, perhaps due to vaccination eligibility expanding among this group later in vaccine roll-out, affording parents more time to consider the benefits of vaccination. Adaptive and dynamic messaging about the strength and durability of infection-induced immunity, and improved efforts to resolve confusion associated with suitable spacing of COVID-19 infection and receipt of COVID-19 vaccination may improve uptake [9].

Table 3
Comparison of vaccination status defined by the California Immunization Registry (CAIR) and vaccination self-report using data from the California COVID-19 case-control study. Characteristics of participants included in this analysis are listed in Table S2.

	CAIR-Vaccinated *N*	CAIR-Unvaccinated *N*	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
A. All participants						
Self-report Vaccinated	817	263	0.82 (0.80, 0.85)	–	0.76 (0.73, 0.78)	–
Self-report Unvaccinated	177	1,774	–	0.87 (0.86, 0.89)	–	0.91 (0.90, 0.92)
B. Use of Recall Aid						
Self-report vaccinated referenced vaccine card	577	180	0.98 (0.97, 0.99)	–	0.76 (0.73, 0.78)	–
Self-report vaccinated with another recall aid (ex. e-mail or calendar)	137	51	0.92 (0.86, 0.96)	–	0.73 (0.66, 0.79)	–
Self-report vaccinated without recall aid	98	32	0.45 (0.38, 0.52)	–	0.75 (0.67, 0.83)	–
C. SARS-CoV-2 Positive						
Self-report Vaccinated	299	74	0.86 (0.82, 0.90)	–	0.80 (0.76, 0.85)	–
Self-report Unvaccinated	48	1098	–	0.94 (0.92, 0.95)	–	0.96 (0.94, 0.97)
D. SARS-CoV-2 Negative						
Self-report Vaccinated	518	189	0.80 (0.77, 0.83)	–	0.73 (0.70, 0.76)	–
Self-report Unvaccinated	129	676	–	0.78 (0.75, 0.81)	–	0.84 (0.81, 0.86)
E. Test Status & Recall Aid						
SARS-CoV-2 Positive						
Self-report vaccinated referenced vaccine card	270	65	0.97 (0.95, 0.99)	–	0.81 (0.76, 0.85)	–
Self-report vaccinated without recall aid	27	9	0.48 (0.35, 0.62)	–	0.75 (0.58, 0.88)	–
SARS-CoV-2 Negative						
Self-report vaccinated referenced vaccine card	444	166	0.97 (0.95, 0.98)	–	0.73 (0.69, 0.76)	–
Self-report vaccinated without recall aid	71	23	0.44 (0.36, 0.51)	–	0.76 (0.66, 0.84)	–

Abbreviations: CAIR = California Immunization Registry; PPV = positive predictive value; NPV = negative predictive value.

We did not identify strong evidence of differences in vaccine uptake among unvaccinated individuals according to race/ethnicity, region of residence, anxiety about COVID-19, or opinions about other COVID-19 preventive strategies. No single set of participant-reported reasons for uncertainty or unwillingness to receive COVID-19 vaccine was associated with likelihood of subsequent vaccine uptake. While our findings identify that uncertainty and unwillingness to receive COVID-19 vaccination is not an absolute barrier to subsequent receipt of vaccination, suboptimal vaccine uptake among unvaccinated individuals who expressed willingness to be vaccinated demonstrate gaps in vaccine delivery and/or outreach efforts in California. Associations of vaccine uptake with household income, among participants expressing both uncertainly/unwillingness and willingness to receive COVID-19 vaccination, underscore the need to promote vaccine access and availability in underserved/low-income communities.

Our study complements cross-sectional studies that have characterized vaccine acceptance over time and across communities throughout the pandemic [11–16]. While surveys of vaccine intent can help policymakers understand determinants of vaccine acceptance, caution must be used in interpreting these estimates because self-reported acceptance may not translate to vaccine uptake in the real world [17,18]. Indeed, 54% of respondents in our study who expressed willingness to receive COVID-19 vaccination had no evidence of receipt of any vaccine doses within the state-wide immunization by late 2021. This observation may indicate social desirability bias, or the tendency to overreport attributes that may be perceived, by the participant, as socially desirable, among the sample of individuals who consented to participant in a telephone-based questionnaires with public health workers [19]. Our findings are similar to those of a cohort study conducted prior to the widespread availability of COVID-19 vaccines, which likewise identified that 46% of participants who initially expressed enthusiasm about COVID-19 vaccination remained unvaccinated at follow-up during March-April 2021 [20]. Linking self-reported vaccine hesitancy or willingness with a comprehensive state-wide vaccine registry provided an opportunity to assess alignment of participants' stated vaccination intentions with real-world vaccine receipt, and to identify predictors of COVID-19 vaccine uptake among participants who initially expressed uncertainty as well as missed opportunities to vaccinate individuals who expressed willingness to receive COVID-19 vaccination.

Few prior studies have assessed the accuracy of self-reported COVID-19 vaccination status. A previous evaluation found agreement between self-reported COVID-19 vaccination status and seropositivity against the SARS-CoV-2 spike protein [20], although such assessments are limited by the fact that seroresponse may also indicate prior infection. Agreement between self-reported vaccination status has been established for other vaccine products, supporting the use of self-reported vaccination status in survey-based research and vaccine effectiveness studies [21]. In our study, specificity of self-reported vaccination status, or the ability to accurately recall not receiving any COVID-19 vaccine doses, was significantly higher than the sensitivity of self-report, or the ability to accurately recall receiving a COVID-19 vaccine dose. Sensitivity of COVID-19 vaccination self-report was notably better among participants referencing a recall aide, especially a COVID-19 vaccination card.

This analysis has several limitations. First, classification of participants with no vaccine record identified in the immunization registry as unvaccinated may be inaccurate; for instance, if individuals received all their vaccine doses outside California. However, this misclassification is likely uncommon, given our study was limited to California residents, recommended intervals between first and second mRNA doses are long, and recommendations for receipt of booster doses were issued during the study period. Second, this study was limited to participants who sought SARS-CoV-2 testing, who may otherwise be more connected to health services and therefore more likely seek vaccination. Third, this analysis evaluated only initiation of the COVID-19 vaccine series which may be an imperfect predictor of willingness to receive subsequent doses needed to maintain or restore immunity to protective levels. Fourth, this analysis was limited to participants who were unvaccinated throughout the study period and therefore does not estimate determinants of vaccine-uptake across the full population in California; however, predictors of vaccine uptake among the unvaccinated remain important to inform public health policies aimed at improving vaccine coverage. Finally, unmeasured confounding may persist [22].

We identified that self-reported vaccination intent was a strong but imperfect predictor of subsequent vaccine initiation. As no single reason for vaccine hesitancy predicted likelihood of vaccine receipt, public health campaigns addressing multiple factors underlying vaccine hesitancy remain important tools to improve acceptance in hesitant populations.

Disclaimer

The findings and conclusions in this article are those of the author(s) and do not necessarily represent the views or opinions of the California Department of Public Health or the California Health and Human Services Agency.

Funding

Centers for Disease Control and Prevention, Epidemiology, and Laboratory Services (US) grant number 5–NU50CK000539.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Jake M. Pry reports financial support was provided by California Department of Public Health Center for Infectious Diseases.].

Acknowledgements

We would like to thank all study participants that gave time to complete our survey making possible this work. We would also like to thank our funders, the United States Centers for Disease Control and Prevention, for supporting this work through the Epidemiology and Laboratory Capacity (ELC) building grant (grant number 5-NU50CK000539).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2023.01.066.

References

[1] Vilches TN, Moghadas SM, Sah P, Fitzpatrick MC, Shoukat A, Pandey A, et al. Estimating COVID-19 infections, hospitalizations, and deaths following the US vaccination campaigns during the pandemic. JAMA Netw Open 2022;5:e2142725. https://doi.org/10.1001/jamanetworkopen.2021.42725.

[2] Omer SB, Benjamin RM, Brewer NT, Buttenheim AM, Callaghan T, Caplan A, et al. Promoting COVID-19 vaccine acceptance: recommendations from the Lancet Commission on Vaccine Refusal, Acceptance, and Demand in the USA. Lancet 2021;398:2186–92. https://doi.org/10.1016/S0140-6736(21)02507-1.

[3] Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, et al. A global survey of potential acceptance of a COVID-19 vaccine. Nat Med 2021;27:225–8. https://doi.org/10.1038/s41591-020-1124-9.

[4] Andrejko KL, Pry J, Myers JF, Jewell NP, Openshaw J, Watt J, et al. Prevention of COVID-19 by mRNA-based vaccines within the general population of California. Clin Infect Dis 2021. https://doi.org/10.1093/cid/ciab640.
[5] Affairs (ASPA) AS for P. COVID-19 Vaccines. HHSGov 2020. Available from: https://www.hhs.gov/coronavirus/covid-19-vaccines/index.html (accessed February 25, 2022).
[6] California S of. Vaccination progress data n.d. Available from: https://covid19.ca.gov/vaccination-progress-data/ (accessed October 19, 2021).
[7] Andrejko KL, Pry J, Myers JF, Openshaw J, Watt J, Birkett N, et al. Predictors of SARS-CoV-2 infection following high-risk exposure. Clin Infect Dis 2021: ciab1040. https://doi.org/10.1093/cid/ciab1040.
[8] Andrejko KL, Pry JM, Myers JF, Fukui N, DeGuzman JL, Openshaw J, et al. Effectiveness of face mask or respirator use in indoor public settings for prevention of SARS-CoV-2 infection — California, February–December 2021. MMWR Morb Mortal Wkly Rep 2022;71:212–6. https://doi.org/10.15585/mmwr.mm7106e1.
[9] León TM. COVID-19 cases and hospitalizations by COVID-19 vaccination status and previous COVID-19 diagnosis — California and New York, May–November 2021. MMWR Morb Mortal Wkly Rep 2022:71. https://doi.org/10.15585/mmwr.mm7104e1.
[10] Schoenfeld D. Partial residuals for the proportional hazards regression model. Biometrika 1982;69:239–41. https://doi.org/10.1093/biomet/69.1.239.
[11] Meyer MN, Gjorgjieva T, Rosica D. Trends in health care worker intentions to receive a COVID-19 vaccine and reasons for hesitancy. JAMA Netw Open 2021;4:e215344. https://doi.org/10.1001/jamanetworkopen.2021.5344.
[12] Mora AM, Lewnard JA, Kogut K, Rauch S, Morga N, Jewell N, et al. Impact of the COVID-19 pandemic and vaccine hesitancy among farmworkers from monterey county, California 2020:2020.12.18.20248518. doi: 10.1101/2020.12.18.20248518.
[13] Skirrow H, Barnett S, Bell S, Riaposova L, Mounier-Jack S, Kampmann B, et al. Women's views on accepting COVID-19 vaccination during and after pregnancy, and for their babies: a multi-methods study in the UK. BMC Pregnancy Childbirth 2022;22:33. https://doi.org/10.1186/s12884-021-04321-3.
[14] Rogers JH, Cox SN, Hughes JP, Link AC, Chow EJ, Fosse I, et al. Trends in COVID-19 vaccination intent and factors associated with deliberation and reluctance among adult homeless shelter residents and staff, 1 November 2020 to 28 February 2021 – King County. Washington Vaccine 2022;40:122–32. https://doi.org/10.1016/j.vaccine.2021.11.026.
[15] Daly M, Robinson E. Willingness to vaccinate against COVID-19 in the U.S.: representative longitudinal evidence from April to October 2020. Am J Prev Med 2021;60:766–73. https://doi.org/10.1016/j.amepre.2021.01.008.
[16] Szilagyi PG, Thomas K, Shah MD, Vizueta N, Cui Y, Vangala S, et al. National trends in the US Public's likelihood of getting a COVID-19 Vaccine—April 1 to December 8, 2020. JAMA 2021;325:396–8. https://doi.org/10.1001/jama.2020.26419.
[17] McEachan RRC, Conner M, Taylor NJ, Lawton RJ. Prospective prediction of health-related behaviours with the Theory of Planned Behaviour: a meta-analysis. Health Psychol Rev 2011;5:97–144. https://doi.org/10.1080/17437199.2010.521684.
[18] Malik AA, McFadden SM, Elharake J, Omer SB. Determinants of COVID-19 vaccine acceptance in the US. EClinicalMedicine 2020:26. https://doi.org/10.1016/j.eclinm.2020.100495.
[19] Holbrook AL, Green MC, Krosnick JA. Telephone versus face-to-face interviewing of national probability samples with long questionnaires: comparisons of respondent satisficing and social desirability response bias. Public Opin Q 2003;67:79–125.
[20] Siegler AJ, Luisi N, Hall EW, Bradley H, Sanchez T, Lopman BA, et al. Trajectory of COVID-19 vaccine hesitancy over time and association of initial vaccine hesitancy with subsequent vaccination. JAMA Netw Open 2021;4:e2126882.
[21] Donald RM, Baken L, Nelson A, Nichol KL. Validation of self-report of influenza and pneumococcal vaccination status in elderly outpatients. Am J Prev Med 1999;16:173–7. https://doi.org/10.1016/S0749-3797(98)00159-7.
[22] Fridman A, Gershon R, Gneezy A. COVID-19 and vaccine hesitancy: a longitudinal study. PLoS One 2021;16:e0250123. https://doi.org/10.1371/journal.pone.0250123.