Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about the work.

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Methods

Study Design and Methodology

Population

The HEROES-RECOVER network consists of the Arizona Healthcare, Emergency Response and Other Essential Workers Surveillance (HEROES) study conducted in Phoenix, Tucson, and other areas, and the Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) study conducted in Florida (Miami), Minnesota (Duluth), Oregon (Portland), Texas (Temple), and Utah (Salt Lake City). Both studies use consistent methods that have been published previously. [1-3] Frontline workers (including healthcare personnel (HCP), first responders (FR), and other essential and frontline workers (EFW) working at least 20 hours per week and having close contact with (within 3 feet) coworkers, customers, patients, or the public as part of their routine work) were eligible for recruitment. To minimize potential selection biases, recruitment of participants was stratified according to site, sex, age group, and occupation with a minimum number of enrollees per stratum, depending on site enrollment targets. All participants provided written informed consent. The individual protocols for the RECOVER study and the HEROES study were reviewed and approved by the institutional review boards at participating sites or under a reliance agreement.

Active Surveillance

Participants self-collect a mid-turbinate nasal specimen using a flocked swab placed in viral transport medium (VTM) on a weekly basis, regardless of whether they had symptoms associated with COVID-19. Participants provide an additional dry foam anterior nasal swab and saliva specimen at the onset of a COVID-19-like illness (CLI). Participants are provided with

training and materials for the self-collection of each specimen type at enrollment. Participants are given written and visual detailed instructions for collecting, storing, and submitting specimens by dropping them off at a specified location, having them picked up by an at-home courier, or shipping them according to guidance and specifications from the US Food and Drug Administration. Supplies and instructions for participants were standardized across sites.

Specimens are shipped on day of collection unfrozen (on ice packs) and tested by means of qualitative reverse-transcriptase—polymerase-chain-reaction (RT-PCR) assay at the Marshfield Clinic Research Institute (Marshfield, WI). Quantitative RT-PCR assays are conducted at the Wisconsin State Laboratory of Hygiene (Madison, WI). SARS-CoV-2 whole-genome sequencing is conducted at the Centers for Disease Control and Prevention, in accordance to previously published protocols[5]. All study sites use a common protocol and data collection instruments approved by their institutional review boards (IRBs), as well as standard operating procedures.

Participant Data Collection

Data collection is conducted using REDCap software (Vanderbilt University, Nashville, TN, USA). Participants report via SMS using the Twilio platform that can directly integrate with REDCap for online surveys. Upon enrollment, participants complete an online survey to provide detailed occupation, sociodemographic, and health characteristics. Approximately every four months, a follow up survey is distributed to update information collected upon enrollment. In addition, these surveys may include assessments of participant knowledge, attitudes, and practices regarding COVID-19 vaccines, adverse reactions to vaccination, and any illnesses that may not have been reported during routine screening.

Active surveillance for symptoms associated with COVID-19 — defined as fever, chills, cough, shortness of breath, sore throat, diarrhea, muscle aches, or a change in smell or taste — is conducted through weekly text messages, emails, and reports obtained directly from the participant or from medical records. When a COVID-19–like illness is identified, participants complete electronic surveys at the beginning and end of the illness to indicate the date of symptom onset, symptoms, temperatures, the number of days spent sick in bed for at least half the day, and the last day of symptoms. Febrile symptoms associated with COVID-19 is defined as fever, feverishness, chills, or a measured temperature higher than 38°C. In the survey, participants report receipt of medical care. Medically attended care is defined as telemedicine, physician office, emergency room, or urgent care encounters, and hospitalizations related to the illness.

In addition to the weekly questions to assess COVID-19–like illness, participants are also asked one of four "rotating" questions, such that each question is asked approximately monthly. Weeks 1-3 ask setting-based questions that report their potential exposure to SARS-CoV-2 and their use of face masks and other employer-recommended personal protective equipment (PPE) according to: hours of close contact with (within 3 feet [1 m] of) others at work (coworkers, customers, patients, or the public) in the previous 7 days; the percentage of time using PPE during those hours of close contact at work; hours of close contact with someone suspected or confirmed to have COVID-19 at work, at home, or in the community in the previous 7 days; and the percentage of time using PPE during those hours of close contact with the virus. The 4th week asks about either worry about COVID-19 infection risk (AZ only) or sleep quality.

Electronic Medical Record (EMR) Data Collection

In the Minnesota, Oregon, Texas and Utah sites, EMR are monitored routinely to identify medical visits for acute respiratory or COVID-19-like illness. EMR data are also extracted to assess chronic medical conditions, influenza and COVID-19 vaccination data.

Laboratory Testing

Real-time RT-PCR

RNA extraction was performed using the MagMAX Viral/Pathogen Nucleic Acid Isolation Kit on the KingFisher Flex system. RT-PCR was performed using the TaqPath™ COVID-19 Combo Kit on the QuantStudio 7 Pro real-time RT-PCR system. Positive specimens were defined as having at least two SARS-CoV-2 targets (ORF1ab, N gene, S gene) with a threshold cycle (Ct) value ≤37 per manufacturer's instructions.[4] Approximately 20% of specimens were randomly selected for re-testing as part of routine quality control testing procedures.

Genetic Sequencing

Available specimens with <32 Ct value by RT-PCR were subjected to SARS-CoV-2 whole genome sequencing by the Illumina MiSeq platform following previously published protocols.[5] Additional RT-PCR amplicon amplification followed by Sanger sequencing was applied to the samples with incomplete genome sequences after initial Miseq sequencing.[5] Consensus sequences were generated with Iterative Refinement Meta-Assembler (IRMA) (IRMA v1.0.2 with LABEL v0.6.3 for Linux & Mac OS X, 03-2021) and the SARS CoV-2 genome sequence lineage call was based on PANGOLIN v2.3.8 (https://github.com/cov-lineages/pangolin). Lineages were categorized as variants of concern, variants of interest, wild type, or other variants according to criteria published by CDC: SARS-CoV-2 Variant Classifications and Definitions:

https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html.

Statistical Analysis

Participant Inclusion

This analysis covers the period from August 26, 2021 until January 22, 2022. Participants were included for analysis if they were participating in surveillance during the study period and did not have a documented SARS-CoV-2 infection prior to this study period. The final analytic sample included 3,241 unique participants across the Delta and Omicron periods. The final analytic period for Delta included 3,163 participants with a median 95% (IQR: 97%-100%) compliance with weekly swabbing. For the Omicron period, 2,831 participants were included with a median 100% (IQR: 86%-100%) swabbing compliance. See **Figures S1a and S1b** for inclusion into each analytic period for Delta and Omicron, and VE Sensitivity Analyses section that addresses the potential for bias due to excluding participants.

Person-time

Person-time was calculated as the total days under surveillance for a given vaccination status during the study period. Person-time for first and second dose started 14 days after vaccine receipt of an mRNA vaccine and person-time for third dose 7 days after vaccine receipt. The interim 14 days and 7 days were censored as indeterminate vaccination status. Participants who received Johnson & Johnson/Janssen COVID-19 vaccine for primary series were censored at the time of vaccination and could contribute only unvaccinated person-time. Participants who received Johnson & Johnson/Janssen COVID-19 vaccine for third dose were censored at the

time of vaccination and could contribute only unvaccinated, first dose, and second dose person-time.

Virus Predominance

The date Omicron became predominant (>50% of cases) per site was determined using state public health department and CDC surveillance data. SARS-CoV-2 positive cases where lineage results were not yet available or not able to be sequenced (cycle threshold <30) were assumed to be Delta if the illness started prior to the Omicron predominance date at their site. If the illness started after the Omicron predominance date, they were assumed to be Omicron. Overall, 132 (21%) of the 627 SARS-CoV-2 infections occurred during co-circulation, of which 18 (14%) could not be sequenced. Sensitivity analyses are described in VE Sensitivity Analyses and indicate minimal impact on VE estimates when excluded from analysis.

Inverse Propensity of Treatment Weighting (IPTW)

Data were broken into weeks and IPTW weights for immunization were calculated with boosted regression trees using baseline socio-demographic information and time-varying self-reported exposure and mask use.[6] Covariates were considered balanced if the standardized mean difference was ≤ 0.2 after weighting. For relative VE, IPTW was calculated using the probability of being three dose immunized compared to two dose immunized. IPTW was estimated separately for the Delta and Omicron predominant periods **(Figures S2a – S2d).**

Cox Model

Hazard ratios were calculated by the Andersen-Gill model and vaccine effectiveness was then calculated as 100%×(1-hazard ratio).[7] Unadjusted VE was calculated as 100%×(1−hazard ratio). Adjusted Cox models were weighted using the stabilized weights and had site, local SARS-CoV-

2 circulation, and occupation as covariates a priori. Covariates that were not balanced after IPTW weighted were also put in the models and kept if they adjusted the estimates by ≥5%. Relative VE models were further adjusted by days since the most recent vaccine dose. Robust standard errors were used to account for the clustering by participant created by the stabilized weights.

Assumption of Proportional Hazard

The proportional hazards assumption was checked for the main and subgroup Cox models by examining correlation between Schoenfeld residuals and time. No evidence of a non-zero slope was found with $p>0.05$ for all tests.

Incidence of SARS-CoV-2

Incidence of SARS-CoV-2 during the Delta and Omicron predominant periods was calculated as the number of SARS-CoV-2 positive infections divided by the number of person-days in each period. There was overlap in Delta and Omicron circulation in December 2021. Cases with confirmed lineage counted towards their lineage even if in the opposite predominate period. (i.e., confirmed Omicron cases and associated person-time that occurred during the Delta predominant period counted towards Omicron). Rate ratio of incidence in the Omicron vs Delta periods was calculated using a Poisson model with log person-days as an offset.

Clinical characteristics of SARS-CoV-2 Cases

Clinical characteristics of unvaccinated RT-PCR confirmed infections were compared by lineage, Delta or Omicron. Cases within 1 week of the Delta predominance date without lineage results were excluded. Percent of asymptomatic cases were compared for all remaining infections. Percent of cases reporting medical care were compared for symptomatic infections

with a completed final illness survey at the time of data cutoff. Odd ratios were calculated using unadjusted logistic regression (**Table S3**).

Handling of Missing Data

All baseline covariates in the propensity models had complete data. Hours of exposure and percent PPE use were answered by participants when applicable. "Not applicable" was used as a valid response in the boosted regression model and all participant data was used.

VE Sensitivity Analysis

Sensitivity analyses were conducted to examine potential (1) attrition bias by adding participants with low participation (≤20% weekly swab submission) back to the study analytic sample. The adjusted VE against Delta changed from 91% (95% CI: 84–95) to 90% (95% CI: 83–95) and against Omicron changed from 60% (95% CI: 43–72) to 61% (95% CI: 43–73). Relative adjusted VE against Delta changed from 86% (95% CI: 69–94) to 84% (95% CI: 60–93) and against Omicron remained unchanged. In this sensitivity analysis, the overall pattern of findings was similar to the primary analyses. To examine potential (2) misclassification bias by treating not sequence-confirmed SARS-CoV-2 infections during co-circulation period as competing risk for the VE against Omicron infection. First, we treated infections that were not sequence-confirmed and had an onset date within 1 week of the Omicron predominance date as a competing risk. Adjusted VE changed from 60% (95% CI: 43–72) to 57% (95% CI: 38–71). Relative adjusted VE changed from 60% (95% CI: 40–73) to 60% (95% CI: 39–73). Second, we expanded to infections within 2 weeks of Omicron predominance. Adjusted VE changed from 60% (95% CI: 43–72) to 53% (95% CI: 27–69). Relative adjusted VE changed from 60% (95% CI: 40–73) to 60% (95% CI: 35–75). In all sensitivity analyses, the VE point estimate was only slightly reduced, but had a substantially wider confidence interval.

Supplemental Results

Figure S1a. CONSORT diagram of HEROES-RECOVER prospective cohort participants: Delta Variant Predominance

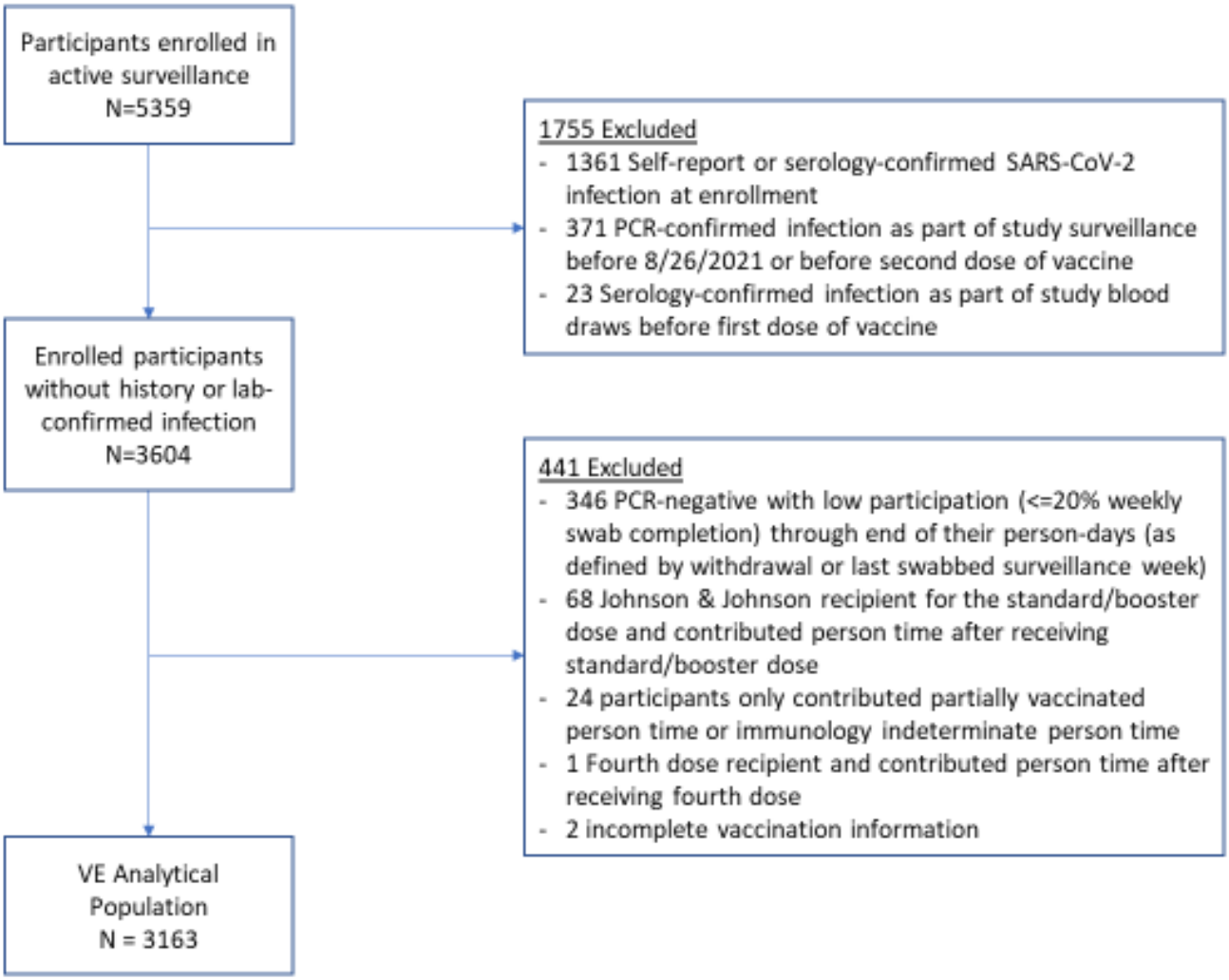


Figure S1b. CONSORT diagram of HEROES-RECOVER prospective cohort participants: Omicron Variant Predominance

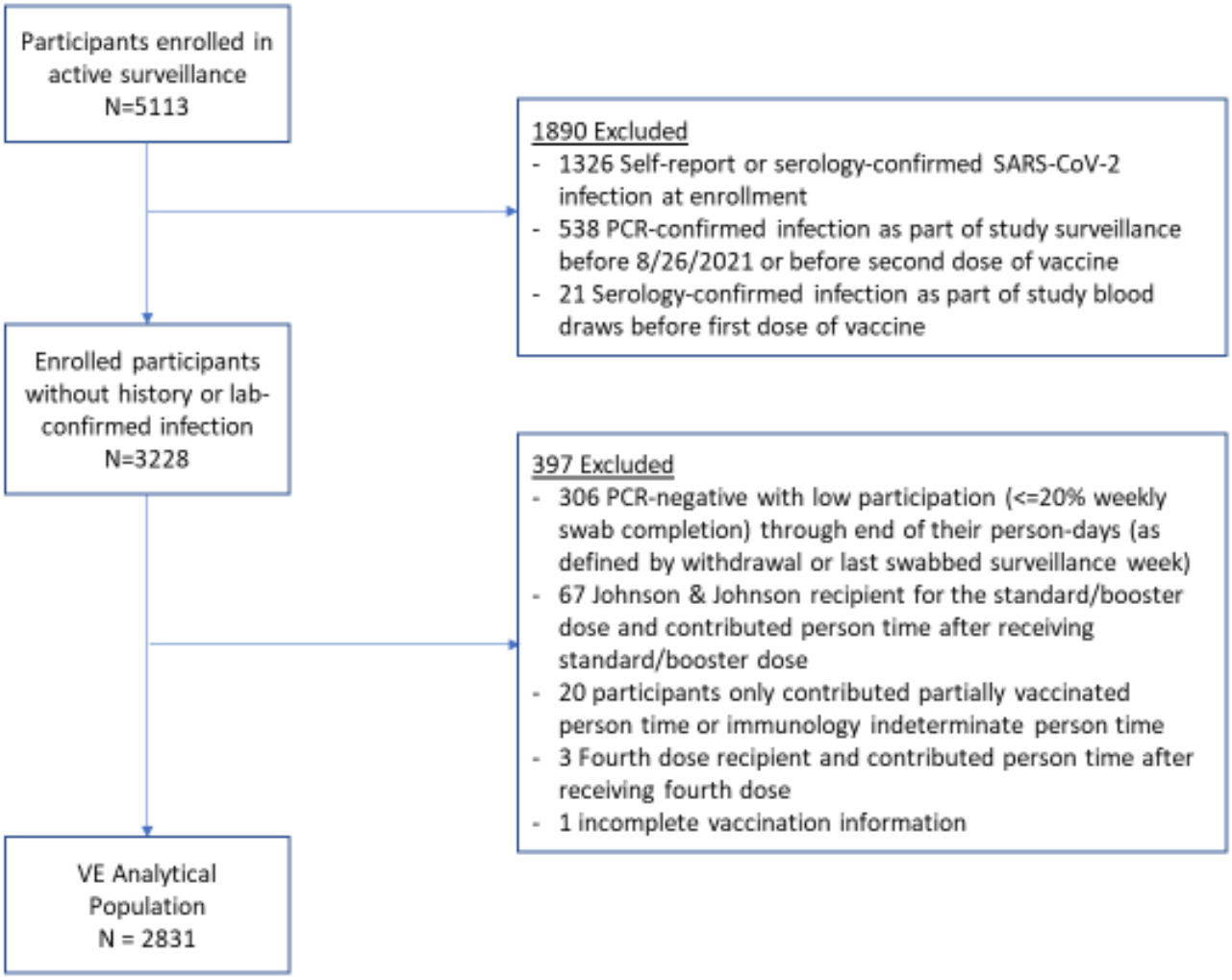


Table S1. Participant characteristics by COVID-19 vaccination status at the end of the study period, August 2021 to January 2022

Characteristic	Total Participants, (Col.%)	SARS-CoV-2 Infection Participants, (Row %)	COVID-19 Vaccination Status		
			Unvaccinated Participants, (Row %)	1- or 2-dose Vaccinated Participants, (Row %)	3-Dose Participants, (Row %)
All Participants	3,241	627 (19.3)	333 (10.3)	1021 (31.5)	1887 (58.2)
Variant predominance period					
B.1.617.2 (Delta)	1855 (57.2)	407 (21.9)	160 (8.6)	606 (32.7)	1089 (58.7)
B.1.1.529 (Omicron)	1386 (42.8)	220 (15.9)	173 (12.5)	415 (29.9)	798 (57.6)
Cohort location					
Phoenix, AZ	308 (9.5)	72 (23.4)	21 (6.8)	121 (39.3)	166 (53.9)
Tucson, AZ	899 (27.7)	163 (18.1)	129 (14.3)	379 (42.2)	391 (43.5)
Other areas in AZ	219 (6.8)	52 (23.7)	41 (18.7)	88 (40.2)	90 (41.1)
Miami, FL	221 (6.8)	76 (34.4)	58 (26.2)	98 (44.3)	65 (29.4)
Duluth, MN	435 (13.4)	73 (16.8)	12 (2.8)	47 (10.8)	376 (86.4)
Portland, OR	457 (14.1)	54 (11.8)	23 (5.0)	54 (11.8)	380 (83.2)
Temple, TX	228 (7.0)	44 (19.3)	14 (6.1)	76 (33.3)	138 (60.5)
Salt Lake City, UT	474 (14.6)	93 (19.6)	35 (7.4)	158 (33.3)	281 (59.3)
Age group, yrs					
18 - 49	2244 (69.2)	457 (20.4)	243 (10.8)	701 (31.2)	1300 (57.9)
≥50	997 (30.8)	170 (17.1)	90 (9.0)	320 (32.1)	587 (58.9)
Sex*					
Female	2036 (62.8)	369 (18.1)	148 (7.3)	636 (31.2)	1252 (61.5)
Male	1200 (37.0)	258 (21.5)	184 (15.3)	384 (32.0)	632 (52.7)
Race†					
White	3073 (94.8)	595 (19.4)	298 (9.7)	952 (31.0)	1823 (59.3)
Other Race	168 (5.2)	32 (19.0)	35 (20.8)	69 (41.1)	64 (38.1)
Ethnicity‖					
Hispanic/Latino	467 (14.4)	111 (23.8)	66 (14.1)	221 (47.3)	180 (38.5)

Other	2774 (85.6)	516 (18.6)	267 (9.6)	800 (28.8)	1707 (61.5)
Occupation					
Primary HCP	700 (21.6)	97 (13.9)	10 (1.4)	124 (17.7)	566 (80.9)
Nurses & other allied HCP	1071 (33.0)	180 (16.8)	67 (6.3)	300 (28.0)	704 (65.7)
First Responders, fire fighters	422 (13.0)	129 (30.6)	104 (24.6)	173 (41.0)	145 (34.4)
First Responders, law enforcement	158 (4.9)	51 (32.3)	39 (24.7)	72 (45.6)	47 (29.7)
Frontline workers, public-facing	675 (20.8)	135 (20.0)	68 (10.1)	265 (39.3)	342 (50.7)
Frontline workers, non-public-facing	215 (6.6)	35 (16.3)	45 (20.9)	87 (40.5)	83 (38.6)
Chronic medical condition					
None	2862 (88.3)	595 (20.8)	311 (10.9)	980 (34.2)	1571 (54.9)
One or more	215 (6.6)	35 (16.3)	45 (20.9)	87 (40.5)	83 (38.6)
Vaccine product			—		
Moderna (mRNA-1273)	887 (27.4)	160 (18.0)	—	439 (9.5)	448 (50.5)
Pfizer-BioNTech (BNT162b2)	1917 (59.1)	330 (17.2)		553 (28.8)	1364 (71.2)
Combination of mRNA products	74 (2.3)	7 (9.5)		0 (0.0)	74 (100.0)

Abbreviations: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), standard mean difference (SMD), messenger RNA (mRNA), healthcare provider (HCP).

* Participants who did not report gender or identified as Other (n=17) were counted in the most common category (female).

† Participants who did not report race (n=4) were counted with Other Race.

‖ Participants who did not report ethnicity (n=77) were counted with Other.

¶ Participants (n=98) who did not provide a response, the data were imputed as none, pending further verification.

Table S2. Distribution of Participant Person-time Contributed to Vaccination Status Categories According to Virus and Participant Characteristics*

Characteristic	Total†		COVID-19 Vaccination Status					
			Unvaccinated		2-Dose (≥14 days after dose 2)		3-Dose (≥7 days after dose 3)	
	Participants No.	Person-days No. (%)	Participants No.	Person-days No. (%)	Participants No.	Person-days No. (%)	Participants No.	Person-days No. (%)
All Participants	3,241	439,411	391	34,956	2,779	236,084	1,801	168,371
Variant predominance period								
B.1.617.2 (Delta)	4,814	337,846 (76.9)	343	27,206 (77.8)	2,764	204,398 (86.6)	1,707	106,242 (63.1)
B.1.1.529 (Omicron)	2,896	101,565 (23.1)	255	7,750 (22.2)	938	31,686 (13.4)	1,708	62,129 (36.9)
Cohort location								
Phoenix, AZ	702	41,166 (9.4)	39	2,645 (7.6)	369	23,482 (9.9)	295	15,039 (8.9)
Tucson, AZ	2,003	120,048 (27.3)	203	11,023 (31.5)	1,083	74,732 (31.7)	719	34,293 (20.4)
Other areas in AZ	472	27,947 (6.4)	65	3,786 (10.8)	244	17,474 (7.4)	163	6,687 (4.0)
Miami, FL	463	27,435 (6.2)	105	6,534 (18.7)	241	16,245 (6.9)	117	4,656 (2.8)
Duluth, MN	1,136	60,418 (13.7)	23	1,586 (4.5)	454	23,967 (10.2)	660	34,865 (20.7)
Portland, OR	1,225	65,622 (14.9)	52	2,694 (7.7)	477	27,359 (11.6)	696	35,569 (21.1)
Temple, TX	529	29,185 (6.6)	27	1,501 (4.3)	271	16,264 (6.9)	231	11,420 (6.8)
Salt Lake City, UT	1,180	67,590 (15.4)	84	5,187 (14.8)	563	36,561 (15.5)	534	25,842 (15.3)
Age group, yrs								
18 - 49	5,302	299,371 (68.1)	429	24,281 (69.5)	2,537	161,018 (68.2)	2,339	114,072 (67.8)
≥50	2,408	140,040 (31.9)	169	10,675 (30.5)	1,165	75,066 (31.8)	1,076	54,299 (32.2)
Sex‡								
Female	4,951	280,186 (63.8)	297	18,352 (52.5)	2,377	148,674 (63.0)	22,80	113,160 (67.2)
Male	2,759	159,225 (36.2)	301	16,604 (47.5)	1,325	87,410 (37.0)	1,135	55,211 (32.8)
Race§								
White	7,355	418,585 (95.3)	546	31,972 (91.5)	3,515	223,612 (94.7)	3,299	163,001 (96.8)
Other Race	355	20,826 (4.7)	52	2,984 (8.5)	187	12,472 (5.3)	116	5,370 (3.2)
Ethnicity ‖								
Hispanic/Latino	1,034	62,557 (14.2)	119	7,346 (21.0)	586	39,650 (16.8)	330	15,561 (9.2)
Other	6,676	376,854 (85.8)	479	27,610 (79.0)	3,116	196,434 (83.2)	3,085	152,810 (90.8)
Occupation								
Primary HCP	1,841	101,003 (23.0)	20	894 (2.6)	771	42,923 (18.2)	1,051	57,186 (34.0)

Nurses & other HCP	2,636	147,766 (33.6)	141	9,262 (26.5)	1,229	73,026 (30.9)	1,269	65,478 (38.9)
First Responders	1,211	71,895 (16.4)	229	12,022 (34.4)	637	46,031 (19.5)	345	13,842 (8.2)
Other essential / frontline workers	2,022	118,747 (27.0)	208	12,778 (36.6)	1,065	74,104 (31.4)	750	31,865 (18.9)
Chronic medical condition[¶]								
None	5,255	300,399 (68.4)	466	27,117 (77.6)	2,546	164,583 (69.7)	2,247	108,699 (64.6)
One or more	2,455	139,012 (31.6	132	7,839 (22.4	1,156	71,501 (30.3	1,168	59,672 (35.4
Vaccine product								
Moderna (mRNA-1273)	2,101	126,762 (28.8)	—	—	1324	96,089 (40.7)	778	30,673 (18.2)
Pfizer-BioNTech (BNT162b2)	4,814	269,735 (61.4)	—	—	2378	139,995 (59.3)	2440	129,740 (77.1)
Combination of mRNA products	197	7,958 (1.8)	—	—	0	0	197	7,958 (4.7)

[*] Abbreviations: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), standard mean difference (SMD), messenger RNA (mRNA), healthcare provider (HCP).

[†] The total number of participants included in this study does not equal the sum of participants shown in each vaccination status category. A participant may contribute to one or more category, since vaccination status is time-varying. For example, a participant who has already received a 3rd vaccine dose at the start of the study period would only contribute person time to the 3-Dose status, thus not appear in the Unvaccinated or 2-Dose categories. A recent vaccinee may contribute person time to both Unvaccinated and 2-Dose person time, thus appearing twice. The purpose of this table is to demonstrate the distribution of person-time contributed by each of the characteristics.

[‡] Participants who did not report gender or identified as Other (n=17, 958 person-days) were counted in the most common category (female).

[§] Participants who did not report race (n=4, 236 person-days) were counted with Other Race.

[‖] Participants who did not report ethnicity (n=77, 4,512 person-days) were counted with Other.

[¶] Participants (5,959 person-days) who did not provide a response, the data were imputed as none, pending further verification.

Table S3. Comparison of SARS-CoV-2 Delta and Omicron variant infection clinical characteristics among unvaccinated HEROES-RECOVER study participants

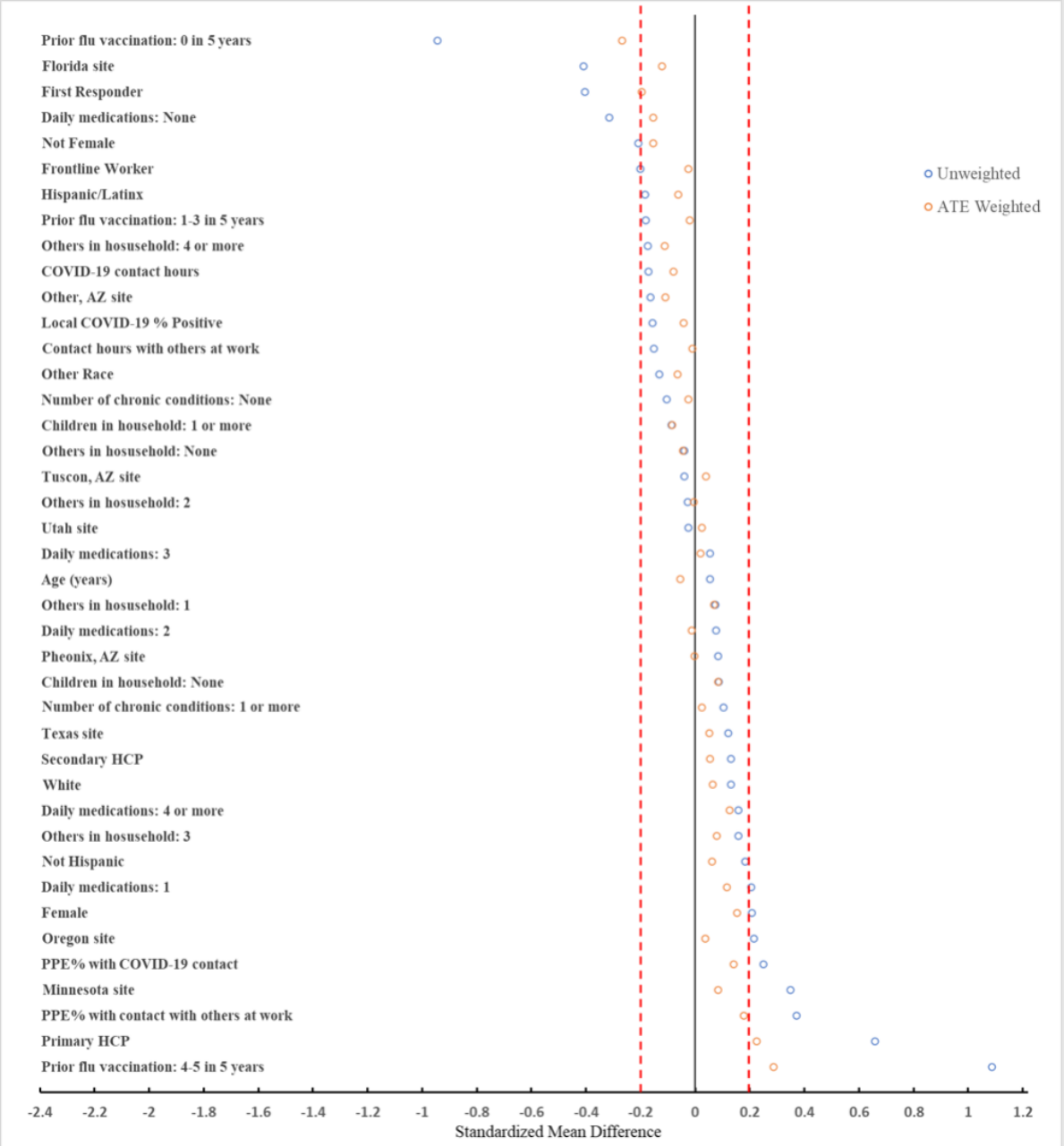
	Total Infections No. (%)	Delta No. (%)	Omicron No. (%)	Odds Ratio*	95%CI
Total participants, no. (%)	131 (100)	51 (100)	80 (100)	--	--
Asymptomatic	21 (16.0)	4 (7.8)	17 (21.3)	0.32	0.10–1.00
COVID-19 symptoms	110 (84.0)	47 (92.2)	63 (78.8)		
Fever	73 (55.7)	33 (70.2)	40 (63.5)	0.85	0.37 -1.93
Cough	80 (61.1)	37 (78.7)	43 (68.3)	0.68	0.28 -1.68
Chills	63 (48.1)	32 (68.1)	31 (49.2)	0.50	0.23 - 1.11
Shortness of breath	23 (17.6)	18 (38.3)	5 (7.9)	0.15	0.05 - 0.43
Sore throat	51 (38.9)	24 (51.1)	27 (42.9)	0.78	0.36 - 1.69
Diarrhea	25 (19.1)	11 (23.4)	14 (22.2)	1.0	0.40 - 2.46
Muscle aches	84 (64.1)	38 (80.9)	46 (73.0)	0.78	0.30 - 1.99
Change in smell or taste	38 (29.0)	29 (61.7)	9 (14.3)	0.11	0.04 - 0.28
Received medical care	32 (24.4)	19 (37.2)	13 (16.3)	0.43	0.18 - 0.99

* Presence of symptoms was assessed by variant type, comparing Delta infections as the referent group to Omicron infections, among unvaccinated participants.

Table S4. Representativeness of HEROES-RECOVER Study Participants

Disease under investigation	SARS-CoV-2 infection and COVID-19 illness
Sex and gender	The HEROES-RECOVER study population is 57% HCP, and correspondingly, predominantly female, which is reflective of the healthcare population.
Age	The HEROES-RECOVER study population is comprised of working adults, predominantly aged <50 years.
Race or ethnic group	Black and Asian populations are underrepresented in the HEROES-RECOVER study population.
Geography	COVID-19 cases vary by different regions in the U.S., of which our cohort only represents 6 states.
Other considerations	The HEROES-RECOVER study population is a highly vaccinated population relative to the general population
Overall representativeness of this study	The HEROES-RECOVER study population is composed of frontline workers such as healthcare workers, first responders, and other essential workers who provide direct care or services to the public placing them at higher risk of exposure to SARS-CoV-2 than the general population. Majority are in the 18-49 age group and white. Depending on the occupation, some occupations are heavily tilted towards a gender (i.e. majority of first responders were male). This multicenter study network consists of workers from 6 states: Arizona, Utah, Minnesota, Oregon, Florida, and Texas.

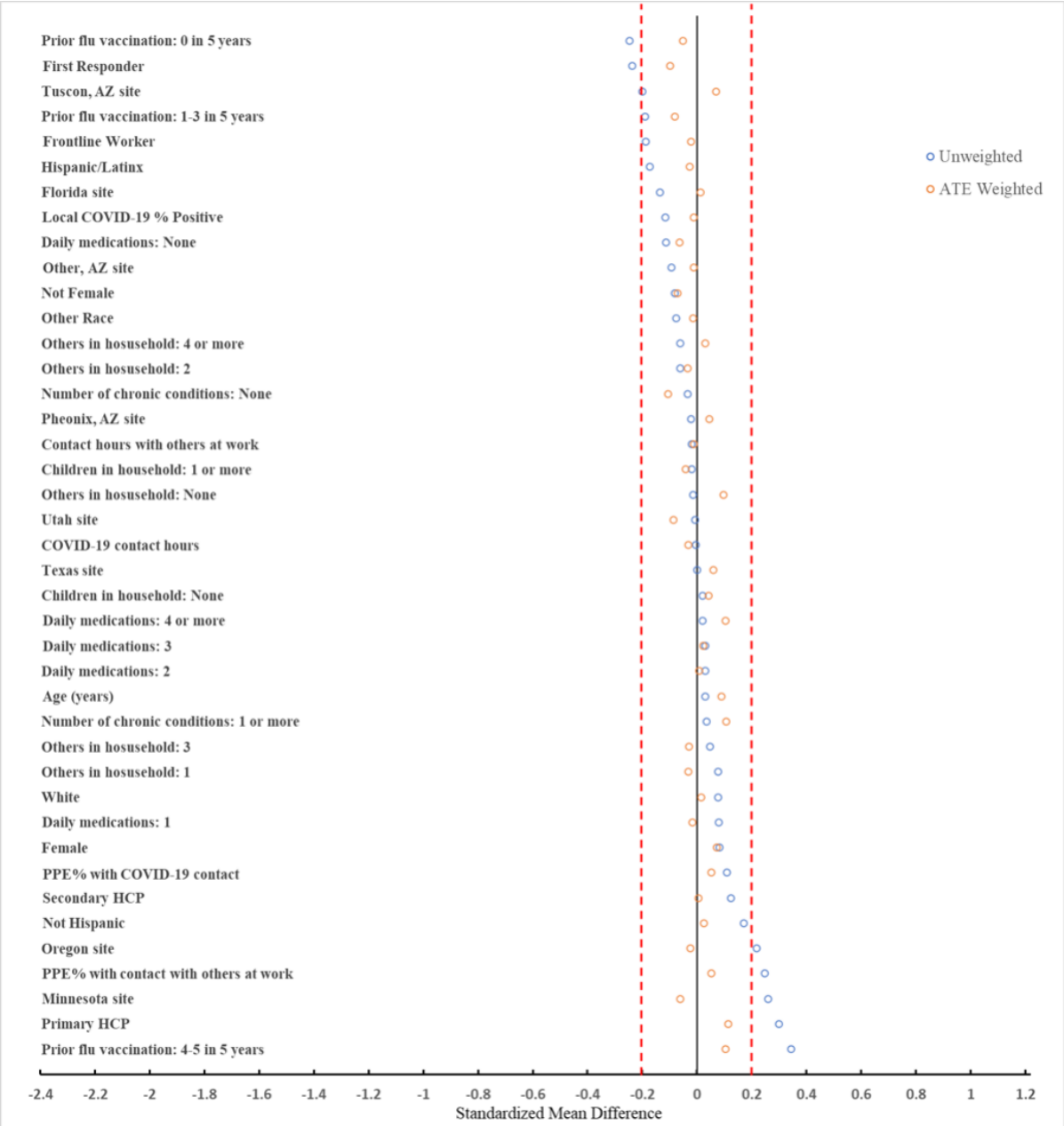
Figure_S2a. Standardized mean differences of covariates between unvaccinated and vaccinated participants during Delta predominance era before and after inverse propensity of treatment weighting



Legend: Negative differences indicate groups that are less likely to be vaccinated and positive differences indicate those more likely to be vaccinated. Absolute standard mean differences of less than 0.2 are considered well balanced. The largest difference after ATE weighting was 0.29.

Abbreviation: Average treatment effect weighted (ATE)

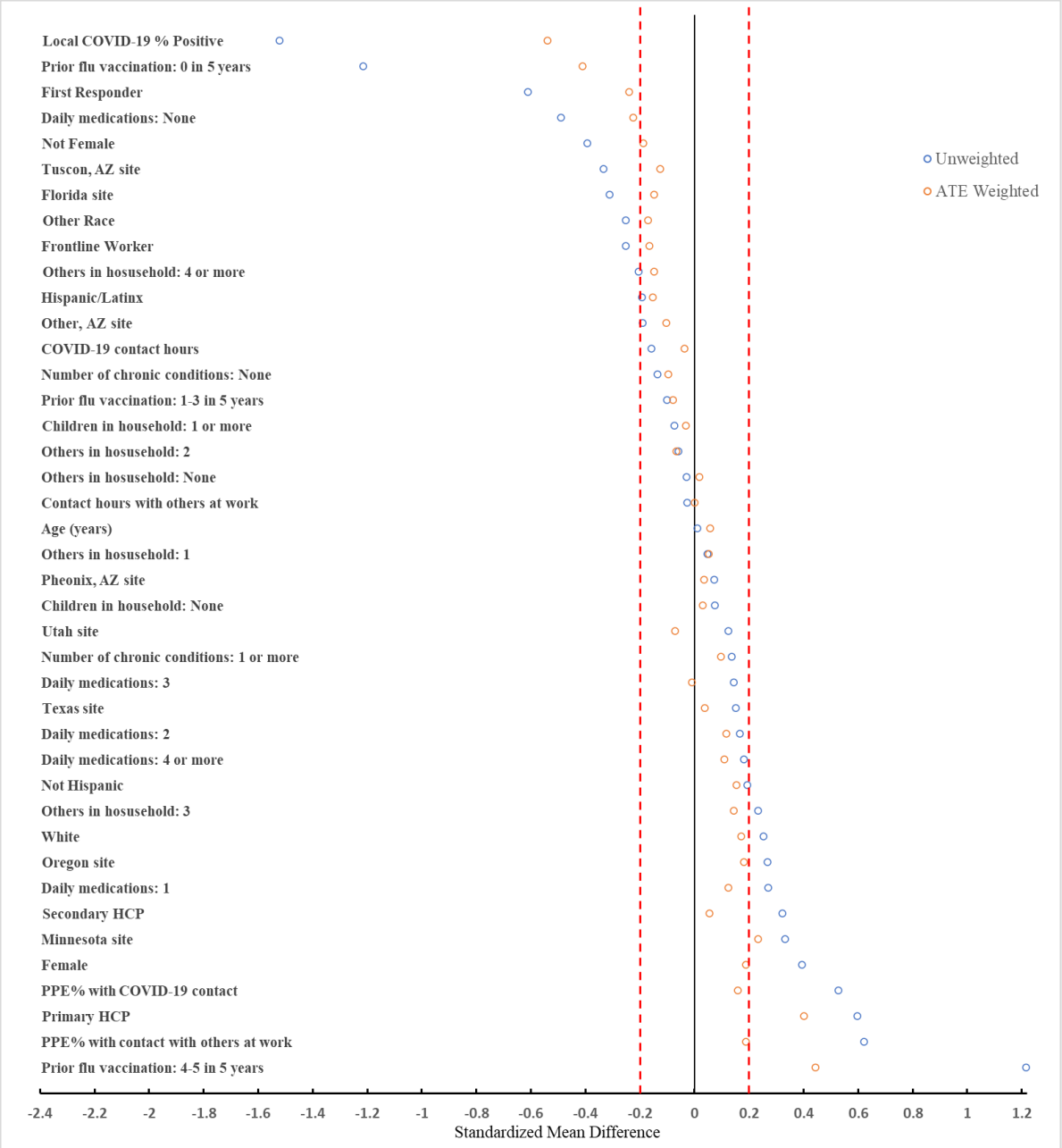
Figure_S2b. Standardized mean differences of covariates between 2-dose and 3-dose vaccinated participants during Delta predominance era before and after inverse propensity of treatment weighting



Legend: Negative differences indicate groups that are less likely to be vaccinated and positive differences indicate those more likely to be vaccinated. Absolute standard mean differences of less than 0.2 are considered well balanced. The largest difference after ATE weighting was 0.11.

Abbreviation: Average treatment effect weighted (ATE)

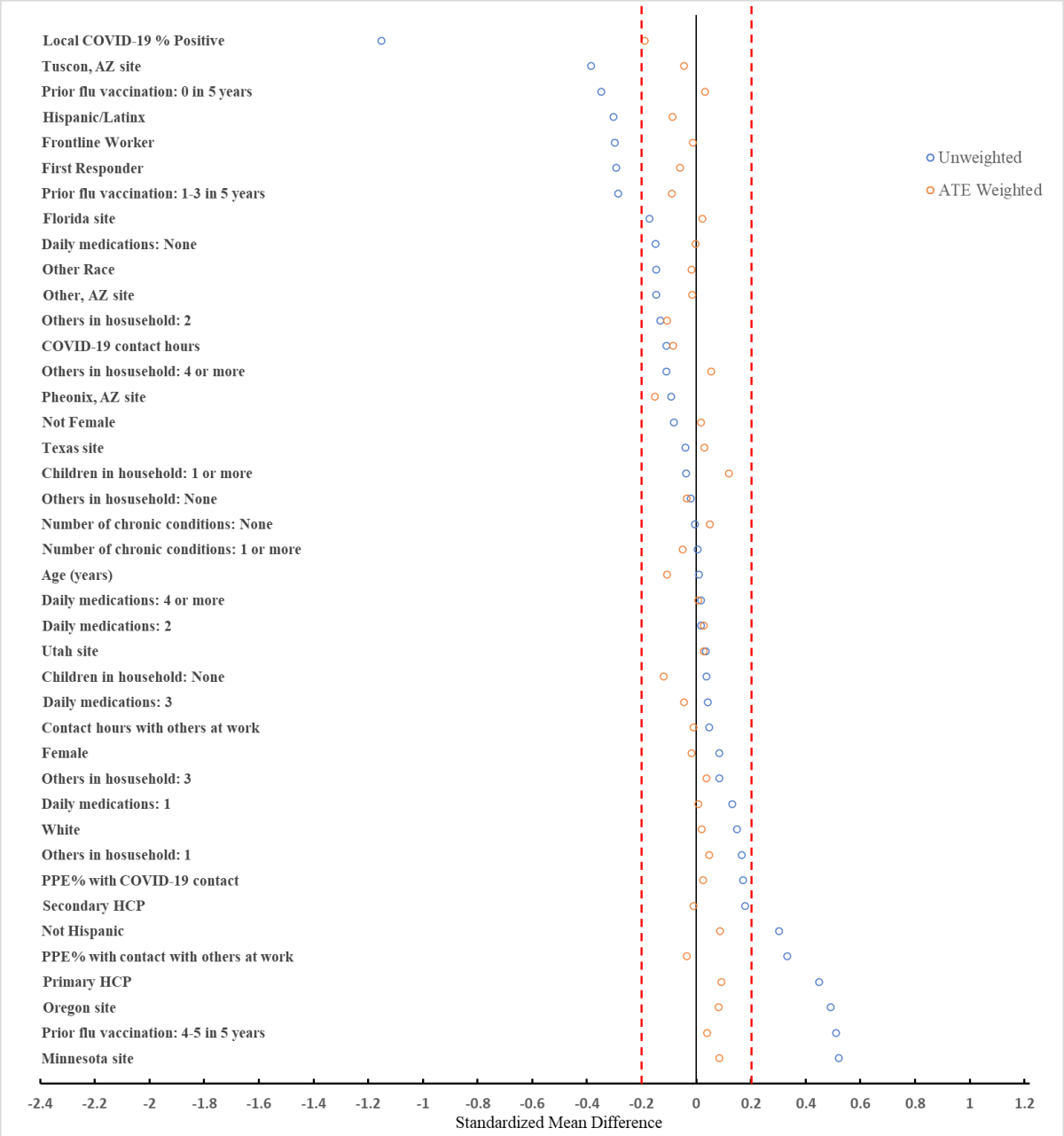
Figure_S2c. Standardized mean differences of covariates between unvaccinated and vaccinated participants during Omicron predominance era before and after inverse propensity of treatment weighting



Legend: Negative differences indicate groups that are less likely to be vaccinated and positive differences indicate those more likely to be vaccinated. Absolute standard mean differences of less than 0.2 are considered well balanced. The largest difference after ATE weighting was 0.54.

Abbreviation: Average treatment effect weighted (ATE)

Figure_S2d. Standardized mean differences of covariates between 2-dose and 3-dose vaccinated participants during Omicron predominance era before and after inverse propensity of treatment weighting



Legend: Negative differences indicate groups that are less likely to be vaccinated and positive differences indicate those more likely to be vaccinated. Absolute standard mean differences of less than 0.2 are considered well balanced. The largest difference after ATE weighting was 0.19.

Abbreviation: Average treatment effect weighted (ATE)

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