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Comparing COVID-19 vaccination coverage, adverse reactions and impact of social determinants of health on vaccine hesitancy in ADRD/MCI and non-ADRD/MCI population: protocol for a retrospective cross-sectional study

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ABSTRACT

Introduction COVID-19 vaccination is crucial for vulnerable people with underlying chronic conditions such as Alzheimer's disease and related dementias (ADRD) and mild cognitive impairment (MCI). These individuals face unique challenges, including higher risk of COVID-19, difficulties in adopting preventive behaviours and vaccine hesitancy due to concerns about adverse reactions. Therefore, efforts to promote vaccination, including boosters tailored to the currently circulating virus, are essential for people with ADRD/MCI.

Objective The primary purpose of this study protocol is to conduct a comprehensive analysis of COVID-19 vaccination coverage and adverse reactions among individuals with ADRD/MCI in comparison to those without ADRD/MCI. Additionally, the proposed study aims to investigate the impact of social determinants of health on COVID-19 vaccination and vaccine hesitancy in individuals with ADRD/MCI.

Methods and analysis A retrospective cross-sectional study will be conducted utilising data from the *All of Us (AoU)* Researcher Workbench. Relevant data fields are extracted from sources including demographic information, COVID-19 Vaccine Survey, Basic Survey, Health Access & Utilization, Social Determinants of Health, and Electronic Health Record (EHR) data. Data on vaccination, adverse reactions and vaccine hesitancy will be collected through COVID-19 vaccine survey questionnaires. Propensity score matching and binary logistic regression will be applied to assess the vaccination rates and vaccine hesitancy, while controlling for demographic characteristics and social determinants of health factors.

Ethics and dissemination This study protocol received approval from the Institutional Review Board at Florida State University (STUDY00004571). Results will be disseminated through publication in peer-reviewed journals and presented at scientific conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A comprehensive study of COVID-19 vaccination rates and hesitancy based on the diverse population and integrated data from electronic health records and COVID-19 panel survey within the *All of Us (AoU)* Research Workbench.
⇒ Over 75% of *AoU* participants are under-represented populations from all 50 states in the USA, which addresses the barriers and vaccine disparities.
⇒ The propensity score matching enables comparable COVID-19 vaccination rates and hesitancy between Alzheimer's disease and related dementias (ADRD)/mild cognitive impairment (MCI) and non-ADRD/MCI cohort by controlling sociodemographic factors, chronic conditions and mental health status.
⇒ One limitation of this proposed study is the limited availability of records pertaining to COVID-19 vaccination boosters, particularly the fourth dose and beyond, in the *AoU* vaccine survey conducted during 2021 and early 2022.

BACKGROUND

COVID-19 vaccines are pivotal in preventing the SARS and long-term symptoms and reducing mortality associated with COVID-19.[1–5] Previous studies have demonstrated the significant association between Alzheimer's disease (AD) and increased risk of COVID-19 infection and mortality.[6 7] Individuals with dementia are particularly vulnerable, facing a two to threefold greater risk of COVID-19 infection partly due to increased levels of angiotensin-converting enzyme 2 compared with the general older adults.[7 8] Additionally, individuals with AD and related dementias (ADRD) encounter challenges in adopting protective behaviours to mitigate infection risks.[9 10]

As COVID-19 vaccine become available, studies on understanding vaccination rates in targeted population have gained significance. Previous studies had compared

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vaccination rates against COVID-19 between different sociodemographic population and chronic conditions. A study focused on community vulnerability found that socioeconomic vulnerability, housing type and composition, and epidemiological factors were associated with at least a 1.0 percentage point decline in county-level vaccination among the US population.[11] Another study in the UK also found that ethnic minority groups had lower age-standardised rates of vaccination compared with the white British population.[12] Mazereel *et al* found that vaccine uptake among people with psychiatric disorders was high and comparable to the general population. However, there still lacks sufficient evidence of comparing vaccination rates among ADRD/mild cognitive impairment (MCI) people.

Increasing vaccination rates play a pivotal role in fostering herd immunity against COVID-19, which serves to curb virus transmission and safeguard those who are more susceptible to COVID-19 adverse consequences.[13] Following the introduction of COVID-19 vaccines, a noticeable reduction in pandemic-related excess deaths was observed among individuals with ADRD.[9] Despite progress, patients with dementia are at a higher risk of breakthrough infections compared with patients without dementia,[14 15] emphasising the importance of accessible booster shots, especially for vulnerable populations with underlying health conditions and comorbidities.[16 17] As of October 2022, 111 367 843 people, equivalent to 34% of the US population, have received booster shots.[18] While patients with ADRD and their caregivers exhibit willingness to facilitate vaccination, a substantial portion of them express concerns about potential adverse events.[19–21] In the example of influenza vaccine, vaccination barriers and hesitancy among patients with dementia include intrapersonal level influences (eg, age, race and ethnicity, income, culture beliefs, dementia-related symptoms), interpersonal level influences (relationships with caregivers, informal caregiver distress) and extrapersonal level influences (media impact, religiosity, living accommodations).[22] Understanding the impact of individual, interpersonal and community-level social determinants on COVID-19 vaccination intent and hesitancy among individuals with ADRD/MCI still requires further exploration.[23 24]

This study aims to provide a comprehensive comparison of vaccination coverage, including at least one dose, two doses and boosters or three full doses, along with adverse reactions between ADRD/MCI individuals and those without ADRD/MCI. Additionally, this study seeks to examine the impact of social determinants of health on COVID-19 vaccination rates and vaccine hesitancy among individuals with ADRD/MCI. By gaining a better understanding of these factors, we can develop targeted strategies to improve vaccination rates and address concerns among this vulnerable population.

OBJECTIVE OF STUDY PROTOCOL

Research aim 1: to determine the difference in COVID-19 vaccination rates (at least one dose, two doses and boosters or three full doses) between ADRD/MCI individuals and those without ADRD/MCI.

Research aim 2: to assess the variation in adverse reactions such as swelling, tiredness, muscle pain, chills, fever, following the COVID-19 vaccination in individuals with ADRD/MCI compared with those without ADRD/MCI.

Research aim 3: to investigate the influence of social determinants of health on COVID-19 vaccination rates and vaccine hesitancy in individuals with ADRD/MCI.

METHODS AND DATA ANALYSIS

Data source: *All of Us (AoU)* Researcher Workbench

The data source for this study protocol will be the *AoU* Researcher Workbench, which is a secure and comprehensive source of biomedical datasets enrolled with a broad, diverse group of US populations.[25 26] The *AoU* Research Workbench seeks to engage individuals from under-represented demographic groups, promoting diversity in research.[27] The *AoU* research programme encompasses various data elements, including participants' basic demographic information, responses to health surveys, physical measurements, biospecimen collection (including blood, urine and saliva samples stored in the secure *AoU* biobank), structured electronic health records (EHRs) and Fitbit tracker data collected from one million participants across the USA.[28] The EHR data are available since *AoU* participants enrolled in the programme in 2018. Each participant has completed informed consent for sharing their EHR data with the data and research centre, and they provide survey responses covering various domains on an ongoing basis.[28 29] Specifically, we will extract relevant data fields from sources such as the Demographics, Basic Survey, COVID-19 Vaccine Survey, Health Access & Utilization, Social Determinants of Health and EHR conditions data. Enrolment for the *AoU* programme commenced in 2018 and is anticipated to continue for at least 10 years. By 2023, the AoU research initiative successfully extended invitations to one million individuals nationwide.[30] The diverse population and data integration from multiple sources within the *AoU* Research Workbench allow for a comparative analysis of vaccination rates, adverse reactions and the influence of social determinants of health on vaccine hesitancy between populations with ADRD/MCI and non-ADRD/MCI populations with a sequential follow-up. The deidentified data are accessible through the *AoU* Researcher Workbench (https://workbench.researchallofus.org) under institutional data use agreements.[31] All analyses will be conducted within a secure platform provided by *AoU* Researcher Workbench. The study protocol and *AoU* materials have received approval from the Institutional Review Board at Florida State University Office of Research.

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Workspace on the *AoU* Researcher Workbench secure platform: ADRD/MCI and COVID-19 vaccination

We have established a workspace named 'ADRD/MCI and COVID-19 vaccination' within the *AoU* Researcher Workbench. This cloud-based platform grants authorised researchers access to and the ability to analyse data from the *AoU*. The platform offers two levels of data access: the registered tier and the controlled tier. We have been granted access to the controlled data tier. Within this controlled tier, we have constructed two distinct cohorts: one consists of individuals with ADRD/MCI and the other consists of those without ADRD/MCI. Cohort formation was based on participants' EHRs, including International Classification of Diseases (ICD) codes related to ADRD/MCI as original source concepts as well as standard concepts group based on the ICD coding and classification. We applied appropriate logical operators such as 'AND' and 'OR' to combine the key inclusion and exclusion criteria. To facilitate our research, we used the dataset builder tool to construct the datasets. Subsequently, we exported the acquired data to Jupyter Notebooks for analysis, leveraging the R programming language V.4.3 (R Foundation for Statistical Computing) and Python V.3.12 (Python Software Foundation).

ADRD/MCI cohort

The ADRD/MCI cohort is formed by gathering information from EHR. Through EHR, individuals are identified for inclusion in the ADRD/MCI cohort if they have been diagnosed with any of the following ICD-9/10 conditions: 'mild cognitive impairment' or 'Alzheimer's disease' or 'dementia' or 'dementia with or without behavioural and psychological symptoms' or 'vascular dementia' or 'Lewy body dementia' or 'frontotemporal dementia'. Deceased people are excluded (online supplemental table 1)

Non-ADRD/MCI Cohort

Individuals who have been diagnosed with MCI or ADRD are excluded. Additionally, deceased people are excluded from this cohort.

Patient and public involvement

There was no patient or public involvement in this research.

Outcome variables

COVID-19 vaccination rates, adverse reactions and vaccine hesitancy will be assessed through EHR drug exposures and COVID-19 Vaccine Survey Questionnaires administered throughout the summer, fall, winter of 2021 and new year 2022. The vaccine survey questionnaires contain inquiries about receiving the first dose/second dose/boosters of COVID-19 vaccination, adverse reactions after vaccination (eg, swelling, fever, headache, muscle pain, etc) and how likely people are to get vaccinated and reasons that make people hesitate to get the vaccine. The respondents will indicate how likely or unlikely they would be vaccinated on a 5-point Likert scale, ranging from 'very likely' to 'very unlikely' (table 1).

Independent variables

Social determinants of health at individual, interpersonal and community-level factors (table 1).

The study protocol encompasses social determinants of health at three levels: individual, interpersonal and community. Individual-level factors include individual demographics, chronic conditions and mental health status. Chronic conditions related to ADRD/MCI and COVID-19 vaccination rates include[32 33] hypertension, cerebrovascular disease, cerebral infarction, overweight and obesity, diabetes, coronary artery disease, heart failure, myocardial infarction, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, cancer and mental health disorders.

Interpersonal-level factors for ADRD/MCI patients consist of sociocultural environment and social support, as assessed in the *AoU* Basic Survey and *AoU* Social Determinants of Health Survey, with affirmative responses to the following questions: (a) 'Do you own or rent the place where you live?' (b) 'Where are you currently living?' (c) 'How many years have you lived at your current address?' (d) 'What is the main type of housing in your neighbourhood?' (e) 'Not including yourself, how many other people live at home with you?' (f) 'how much you agree or disagree that people around here are willing to help their neighbour?' and (g) 'how much you agree or disagree that people in your neighbourhood generally get along with each other?'.

Community-level factors include healthcare facility accessibility and utilisation, as assessed in the *AoU* Health Access & Utilization Survey, with affirmative responses to the following questions: (a) 'During the past 12 months, were you told by a healthcare provider or doctor's office that they did not accept your healthcare coverage?' (b) 'What kind of place that you usually go to when you are sick or need advice about your health?' (c) 'Have you seen any of the following doctors or healthcare providers about your own health in the last 12 months?'—a general doctor; a nurse practitioner; a doctor specialised in women's health; a mental health professional; an optometrist; a podiatrist; a chiropractor; a physical therapist; a dentist; a medical doctor; traditional healers; (d) 'Have you delayed getting care for any of the following reasons in the past 12 months?'—did not have transportation; live in the rural area where distance to healthcare provider is too far; nervous about seeing a healthcare provider; could not get time off work; could not get child care; could not get elderly care; could not afford the copay; could not afford the deductible; had to pay out of pocket for some or all of the procedure.

Samples

We have set up study cohorts and preliminary datasets within the *AoU* Researcher Workbench to assess the availability of essential variables for this study protocol. After conducting an initial screening within the *AoU* Researcher Workbench, we have identified a sample size of 157 281 individuals with COVID-19 vaccination

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Table 1 Measurement matrix

	Study variables	Measure	Data source
Outcomes	Vaccination rates	Did you receive the first dose, second dose and boosters of the COVID-19 vaccination: yes; no; not sure; skip. EHR drug exposure with SARS-COV-2 (COVID-19) vaccination records.	*AoU* COVID-19 Vaccine Survey *& AoU* EHR Drug exposures
	Adverse reactions	Adverse reactions include swelling, fever, Guillain-Barre syndrome, headache, tiredness, muscle pain, chills, nausea, severe allergic reaction (anaphylaxis).	*AoU* COVID-19 Vaccine Survey
	Vaccine hesitancy	When a COVID-19 vaccine is available, how likely are you to get vaccinated: very likely; likely; i do not know yet; unlikely; very unlikely; skip.	*AoU* COVID-19 Vaccine Survey
Cohorts	ADRD/MCI and non-ADRD/MCI	ICD-9/10 diagnosed conditions such as 'mild cognitive impairment' or 'Alzheimer's disease' or 'dementia', or positive responses related to ADRD/MCI diagnosis in the EHR data.	*AoU* EHR Conditions
Individual level factors	Demographics	Age, sex at birth, gender, race, ethnicity.	*AoU* Basic Survey
	Chronic conditions	Chronic conditions related with ADRD/MCI and mental health status: hypertension, cerebrovascular disease, cerebral infarction, overweight and obesity, diabetes, coronary artery disease, heart failure, myocardial infarction, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, cancer, anxiety, major depressive disorder, bipolar disorder, psychotic disorder, sleep disorder	*AoU* EHR Conditions
Interpersonal level factors	Sociocultural environment and social support	Living status, type of residence, household and neighbourhood environment, years of living at residency.	*AoU* Social Determinants of Health Survey *& AoU* Basic Survey
Community level factors	Healthcare accessibility and utilisation	Healthcare insurance coverage accepted by healthcare providers, place for healthcare services, number of visits for general doctors, nurse practitioners, physician assistants, obstetricians/gynaecologists, midwives, and reasons for delayed medical care.	*AoU* Health Access & Utilization Survey

ADRD, Alzheimer's disease and related dementias; AoU, All of Us; EHR, Electronic Health Record; MCI, mild cognitive impairment.

information in either EHR drug exposures domain or the COVID-19 vaccine survey. Among these individuals, 9718 (6%) were diagnosed with ADRD/MCI conditions, and the remaining 110 355 without ADRD/MCI conditions; 37 208 individuals without EHR data are excluded. Through 1:1 propensity score matching, 9718 individuals without ADRD/MCI are paired with 9718 individuals with ADRD/MCI via balancing the demographics, chronic diseases and mental health status (figure 1 and table 2).

Sample size and power calculation

A two-group retrospective cohort design is used in this study protocol. The sample size calculation is powered by the outcomes. The changes in vaccination rate and vaccination hesitancy will be compared between the ADRD/MCI groups and individuals without ADRD/MCI. Hence, there will be a total of two statistical tests conducted. We will follow the methodology proposed by Kelley and Maxell to estimate the sample size for survey questions.[34] Based on the study parameters, a sample size of 2000 was determined sufficient to achieve a conjunctive power of 0.8 or higher at a significance level 0.05.[21]

Statistical analysis plan

Demographic variables will be summarised using descriptive statistics (eg, Mean±*SD* or median with IQR) as appropriate for continuous variables. Frequency and percentage will be summarised for categorical variables. Data quality will be checked, including steps like outlier detection.[35] The distribution of all variables will be examined to check the validity of distribution assumptions before subsequent analyses, using univariate/multivariate Shapiro-Wilk test and a visual inspection of histograms and quantile-quantile plots. If the normal assumption of continuous variables is not met, appropriate data transformations or alternative data analysis procedures (eg, nonparametric, bootstrapping) will be employed. The baseline demographics and survey answers of the ADRD/MCI and without ADRD/MCI cohorts will be summarised in forms of tables and figures, with reporting the corresponding p

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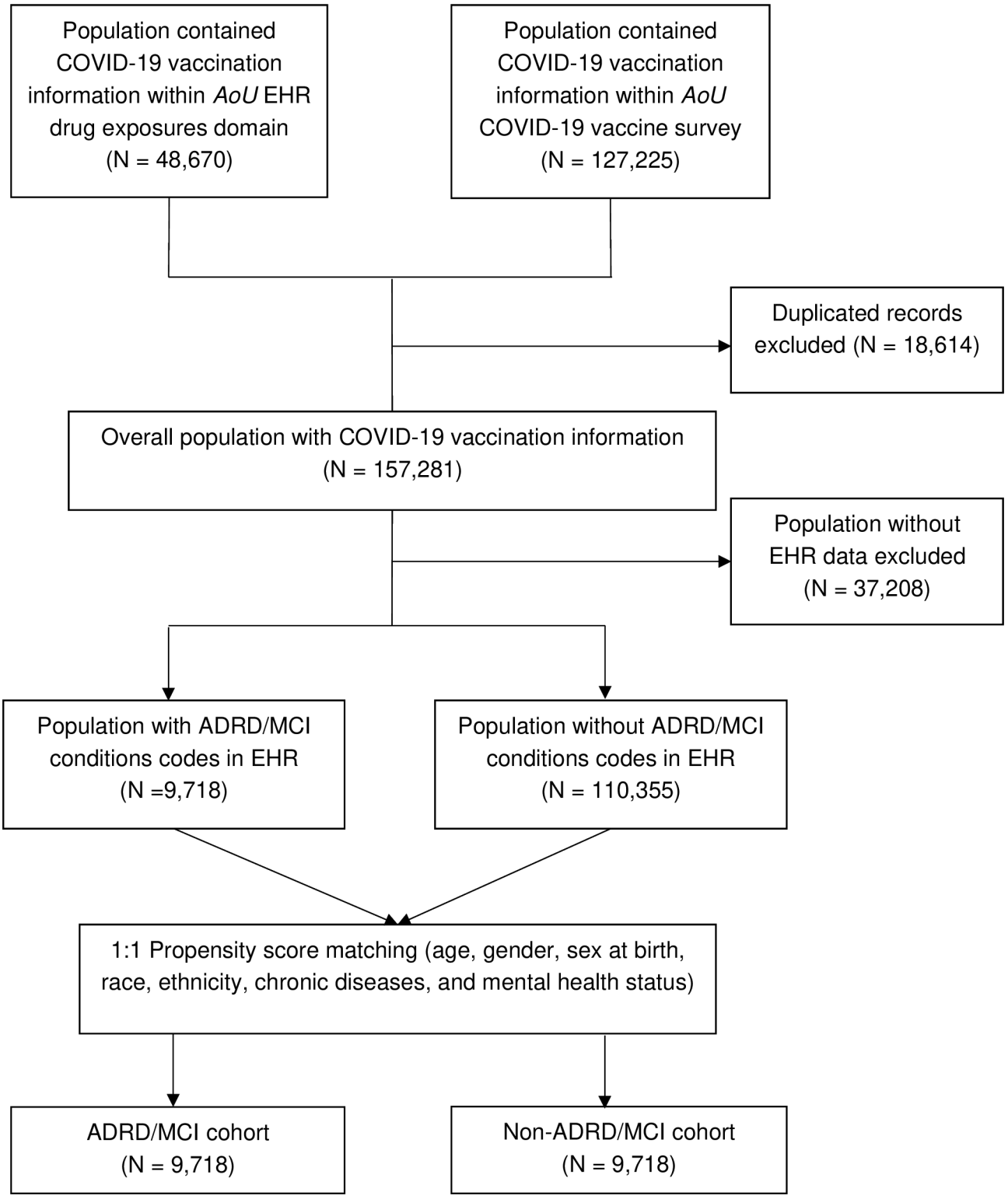

Figure 1 Study flowchart of participants in ADRD/MCI and non-ADRD/MCI cohorts. ADRD, Alzheimer's disease and related dementias; *AoU All of Us;* EHR, Electronic Health Record; MCI, mild cognitive impairment.

values from independent samples t-test (or Kruskal-Wallis test when appropriate) for continuous variables and χ^2 test for categorical variables. Significance level at 0.05 sets as threshold.

In our planned analysis of vaccination rates between ADRD/MCI individuals and those without ADRD/MCI, we use propensity score matching to evaluate the vaccination rate difference between the two cohorts while controlling the selected covariates. Propensity score matching is a statistical matching technique used with observational data, which attempts to construct a balanced intervention and control group by matching

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Table 2 Demographic characteristics, chronic diseases and mental health status of ADRD/MCI and non-ADRD/MCI cohorts before 1:1 propensity score matching, all of us research workbench

Demographics	ADRD/MCI cohort (N=9718)	Non-ADRD/MCI cohort (N=110 355)
Age, N (%)		
18–44	771 (8)	25 410 (23)
45–64	2712 (28)	36 463 (33)
>65	6235 (64)	48 482 (44)
Gender, N (%)		
Male	3663 (38)	38 457 (35)
Female	5745 (59)	68 807 (62)
Other (non-binary, transgender, additional options, prefer not to answer)	90 (1)	920 (1)
Skip or unknown	220 (2)	2171 (2)
Sex at birth, N (%)		
Male	3680 (38)	38 679 (35)
Female	5773 (59)	69 254 (63)
Other (none, intersex, prefer not to answer)	7 (<1)	84 (<1)
Skip or unknown	258 (3)	2338 (2)
Race, N (%)		
White	6632 (68)	72 830 (66)
Black or African American	1180 (12)	14 290 (13)
Asian	143 (2)	2909 (3)
Middle Eastern or North African	49 (<1)	548 (<1)
Native Hawaiian or Other Pacific Islander	4 (<1)	65 (<1)
Multiple-racial	156 (2)	1811 (2)
Other (none indicated, prefer not to answer)	1235 (13)	15 036 (14)
Skip	319 (3)	2866 (3)
Ethnicity, N (%)		
Hispanic or Latino	1166 (12)	15 849 (14)
Non-Hispanic or Latino	8034 (83)	90 266 (82)
Other (none of these, prefer not to answer)	199 (2)	1374 (1)
Skip	319 (3)	2866 (3)
Chronic conditions, N (%)		
Hypertension	7033 (72)	49 455 (45)
Coronary artery disease	2741 (28)	13 464 (12)
Cerebrovascular diseases	3086 (32)	7162 (6)
Heart failure	1962 (20)	8596 (8)
Myocardial infarction	1172 (12)	4998 (5)
Cerebral infarction	1181 (12)	3010 (3)
Overweight/obesity	4784 (49)	34 230 (31)
Diabetes	3498 (36)	21 586 (20)
Chronic obstructive pulmonary disease	1859 (19)	8318 (8)
Chronic kidney diseases	2010 (21)	9871 (9)
Chronic liver diseases	1198 (12)	6030 (5)
Cancer	3613 (37)	23 945 (22)
Mental health status		
Anxiety	5913 (61)	32 843 (30)
Major depressive disorders	6012 (62)	30 200 (27)
Bipolar disorders	1126 (12)	4381 (4)
Psychotic disorders	902 (9)	2676 (2)
Sleep disorders	6306 (65)	33 012 (30)

ADRD, Alzheimer's disease and related dementias; MCI, mild cognitive impairment.

each intervention unit with a controlled unit of similar characteristics.[36] The propensity score is a balancing score, the distribution of baseline covariates will be similar between cohorts.[37] In this retrospective observational study, the cohorts of ADRD/MCI and non-ADRD/MCI individuals are not randomly selected, leading to an imbalance sample sizes and uncontrolled baseline characteristics. This imbalance may cause confounding effects on the vaccination rates. To control the confounding effects, we generate propensity scores using logistic regression to identify the effects of confounding covariates, with the nearest available Mahalanobis metric matching applied to obtain 1:1 matched pair between ADRD/MCI and non-ADRD/MCI cohorts. The balanced covariates in the propensity score matching include age, gender, sex at birth, race, ethnicity, chronic diseases and mental health status. The goal of propensity score matching is to achieve a balanced distribution of covariates between the ADRD/MCI and non-ADRD/MCI groups. We assess the effectiveness of matching by comparing the effective size of each included covariate before and after matching, with a decrease in effective size indicating balanced pairs. The results of propensity logit will be presented in the histogram, and standardised mean differences across covariates before and after matching are reported. The study uses the 'psmpy 0.3.13' propensity score matching package for propensity logits and graphical representations of matching outcomes as well as matched pairs and standardised mean differences across covariates.[38]

Vaccine hesitancy will be computed and compared across cohorts using χ^2 tests. To analyse the association of vaccine hesitancy (ie, individuals reported how likely

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to get vaccinated) with covariates, we will employ a binary logistic regression with vaccine hesitancy as the outcome (5-point Likert scale recategorised to binary outcome: likely or unlikely) and covariates as controlled variables. This approach will enable us to compute the adjusted ORs (AOR) to determine the likelihood of vaccine hesitancy.[39] An AOR greater than 1 indicates higher odds for vaccine hesitancy, meaning individuals who are unlikely to take the vaccination have high vaccine hesitancy.[39] Of 95% CIs for each coefficient's AORs will be calculated. The statistical analysis is performed on Jupyter Notebooks, leveraging the R programming language V.4.3 (R Foundation for Statistical Computing) and Python V.3.12 (Python Software Foundation).

Data management and safety

All datasets will be stored on *AoU* Research Benchwork. Data filtering will be performed on the *AoU* Research platform. Data will be analysed using R or Python. Our research team has experience using Python programming language and has pilot cohorts developed in the *AoU* Research platform and used for analysis. We will adhere to *AoU* research benchwork data protection regulations and data use guidelines.

DISCUSSION

As of May 2023, at least 270 227 181 individuals, constituting 81% of the US population, have received at least one COVID-19 vaccine dose. Furthermore, 230 637 348 people, equivalent to 70% of the population, have achieved full vaccination status.[18] This high rate is considered a highly positive development against the COVID-19 pandemic, due to the vulnerability of older adults with underlying chronic diseases who are at a great risk of severe complications.[40]

The authors compared the cohort of diagnosed ADRD individuals in the *AoU* research dataset to the ADRD prevalence in the US population from the CDC and the 2024 Alzheimer's Disease Facts and Figures Report. According to the 2024 Alzheimer's Association Facts and Figures Report, approximately 6.9 million older adults aged over 65 have been diagnosed with ADRD,[41] along with about 200 000 individuals under age 65 with younger-onset dementia,[42] totalling around 7.1 million diagnosed individuals. This represents approximately 2% of the total US population of 333.3 million. Our findings align with these statistics: in the *AoU* research dataset, we identified 9718 participants diagnosed with ADRD and COVID-19 vaccination records out of a total of 410 235 enrolled *AoU* participants, representing 2% of the overall population. The distribution of chronic conditions in the ADRD cohort in our study, such as hypertension, diabetes and cardiovascular disease, closely aligns with the statistics presented in the Alzheimer's Association's chronic diseases and dementia factsheet.[32] These findings enhance the generalisability of our sample to the broader US population with ADRD.

Individuals with ADRD/MCI had a higher age compared with those without ADRD/MCI. Among the 9718 ADRD/MCI patients, 8% were aged 18–44 (n=771), 28% were aged 45–64 (n=2712) and 64% were aged over 65 (n=6235). In the case of the 110 355 non-ADRD/MCI patients, 23% were aged 18–44 (n=25 410), 33% were aged 45–64 (n=36 463) and 44% were over 65 years old (n=48 482). Individuals with ADRD/MCI had higher rates of chronic conditions and mental health disorders. In comparison to the non-ADRD/MCI cohort, patients with ADRD/MCI had higher prevalence of hypertension, heart diseases, cerebrovascular diseases, overweight/obesity, diabetes, chronic pulmonary diseases, chronic kidney and liver diseases, and cancer. These findings align with reports from the Alzheimer's Association and other previous research.[32 43] Additionally, studies indicate that obesity has become the top risk factor for dementia in the USA.[44] Individuals with ADRD/MCI also displayed a higher prevalence of mental health disorders compared with those without ADRD/MCI.

The proposed study will contribute to scientific knowledge in several ways: first, it will be a comprehensive analysis of vaccination coverage for individuals with ADRD/MCI by examining the first, second and booster shots. This in-depth examination will shed light on any significant differences in vaccination behaviour and adverse reactions between individuals with ADRD/MCI and those without. Such comparisons can provide insights into the unique challenges faced by individuals with ADRD/MCI. This is particularly important where booster shots have become a critical component of maintaining immunity, this comprehensive study can provide insights into long-term vaccination behaviours and trends. Second, this proposed study will assess adverse reactions to COVID-19 vaccines among individuals with ADRD/MCI and those without. This information can offer valuable data on the safety and tolerability of vaccines in vulnerable populations. Healthcare professionals can then make more informed decisions about vaccine administration and monitoring. Third, the proposed study will integrate social determinants of health into its analysis, recognising the potential influence of social determinants of health on vaccination rates is crucial. Equitable vaccination plays an important role in mitigating health-related disparities among minority groups. This proposed study goes beyond the clinical aspect and delves into the broader factors affecting healthcare access and decision-making. Finally, the research findings will directly inform public health strategies and interventions. The research findings can directly inform public health strategies and interventions. If it is found that individuals with ADRD/MCI are more hesitant to receive booster shots, public health strategies can be tailored to address their specific concerns and needs. Policymakers and healthcare providers can use the study's results to make evidence-based decisions regarding vaccine distribution, outreach and support for individuals with ADRD/MCI.

A limitation of this proposed study is the availability of records pertaining to COVID-19 vaccination boosters,

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particularly the fourth dose and beyond are limited in the repeated *AoU* vaccine surveys conducted during the summer, fall, winter of 2021 and new year 2022. Additionally, missing data on EHR records may influence the sample size and power of the analysis, serving as another limitation. To address potential recall bias of adverse reactions associated with COVID-19 vaccination, the four repeated standardised surveys conducted every 3 months allowed us to cross-validate reported adverse events at different time points and reduce the likelihood of recall bias. Additionally, we will verify participants' EHR condition codes for adverse events to ensure accuracy and completeness.

Overall, the proposed study will contribute to scientific knowledge by providing a comprehensive analysis of vaccination coverage, adverse reactions and social determinants of health among individuals with ADRD/MCI. The insights gained from this study can inform public health strategies and interventions, improve vaccine administration and monitoring in vulnerable populations, and help address healthcare disparities.

ETHICS AND DISSEMINATION

This study protocol has obtained the approval from the Institutional Review Board at Florida State University Office of Research (STUDY00004571). This secondary research utilised deidentified pre-existing data. Findings will be published in peer-reviewed journals and disseminated at conferences and through social media.

Contributors YY conceived the idea for the study. YY, JW, HJP, CL and DS drafted, participated in manuscript editing and study design. YY, CL and DS performed the acquisition and interpretation of data for the work. All authors reviewed the study critically, accountable for all aspects of the work, and approved the study protocol. YY serves as the guarantor and accepts the responsibility for the overall content.

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