Title: Racial, Ethnic, and Rural Disparities in US Veteran COVID-19 Vaccine Rates

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- We performed a retrospective cohort study of more than 5.7 million veterans
- Primary outcome: uptake of first COVID-19 vaccine in the first phase of allocation
- Black, Hispanic, and AA/PI Veterans were more likely to receive a vaccine
- Veterans in rural areas were less likely than urban Veterans to receive a vaccine

ABSTRACT:

Background: Race, ethnicity, and rurality-related disparities in coronavirus disease 2019 (COVID-19) vaccine uptake have been documented in the United States (US).

Objective: We determined whether these disparities existed among patients at the Department of Veterans Affairs (VA), the largest healthcare system in the US.

Design, Settings, Participants, Measurements: Using VA Corporate Data Warehouse data, we included 5,871,438 patients (9.4% women) with at least one primary care visit in 2019 in a retrospective cohort study. Each patient was assigned a single race/ethnicity, which were mutually exclusive, self-reported categories. Rurality was based on 2019 home address at the zip code level. Our primary outcome was time-to-first COVID-19 vaccination between December 15, 2020-June 15, 2021. Additional covariates included age (in years), sex, geographic region (North Atlantic, Midwest, Southeast, Pacific, Continental), smoking status (current, former, never), Charlson Comorbidity Index (based on ≥1 inpatient or two outpatient ICD codes), service connection (any/none, using standardized VA-cutoffs for disability compensation), and influenza vaccination in 2019-2020 (yes/no).

Results: Compared with unvaccinated patients, those vaccinated (n=3,238,532; 55.2%) were older (mean age in years vaccinated=66.3, (standard deviation=14.4) vs. unvaccinated=57.7, (18.0), p<.0001)). They were more likely to identify as Black (18.2% vs. 16.1%, p<.0001), Hispanic (7.0% vs. 6.6% p<.0001), or Asian American/Pacific Islander (AA/PI) (2.0% vs. 1.7%, P<.0001). In addition, they were more likely to reside in urban settings (68.0% vs. 62.8, p<.0001). Relative to non-Hispanic White urban Veterans, the reference group for race/ethnicity-urban/rural hazard ratios reported, all urban race/ethnicity groups were associated with increased likelihood for vaccination except American Indian/Alaskan Native (AI/AN) groups. Urban Black groups were 12% more likely (Hazard Ratio (HR)=1.12 [CI 1.12-1.13]) and rural Black groups were 6% more likely to receive a first vaccination (HR=1.06 [1.05-1.06]) relative to white urban groups. Urban Hispanic, AA/PI and Mixed groups were more likely to receive vaccination while rural members of these groups were less likely (Hispanic: Urban HR=1.17 [1.16-1.18], Rural HR=0.98 [0.97-0.99]; AA/PI: Urban HR=1.22 [1.21-1.23], Rural HR=0.86 [0.84-0.88]). Rural White Veterans were 21% less likely to receive an initial vaccine compared with urban White Veterans (HR=0.79 [0.78-0.79]). AI/AN groups were less likely to receive vaccination regardless of rurality: Urban HR=0.93 [0.91-0.95]; AI/AN-Rural HR=0.76 [0.74-0.78].

Conclusions: Urban Black, Hispanic, and AA/PI Veterans were more likely than their urban White counterparts to receive a first vaccination; all rural race/ethnicity groups except Black patients had lower likelihood for vaccination compared with urban White patients. A better understanding of disparities and rural outreach will inform equitable vaccine distribution.

Key Words: COVID-19, Vaccine, Health Disparities, Veterans

Introduction:

Disparities related to coronavirus disease 2019 (COVID-19) are present in the United States (US) with race/ethnicity (RE) and rurality influencing likelihood of vaccination, illness, and mortality. In the first months of the pandemic, data from the Center for Disease Control and Prevention (CDC) showed that Black and Hispanic adults were more likely to test positive, be hospitalized, and die from the virus(1-3). However, early evidence from the Department of Veterans Affairs (VA) – the largest integrated healthcare system in the US – demonstrated that such disparities were attenuated among Veterans in VA care, substantiating previous observations that health disparities tend to be smaller in the VA than in the private sector(4, 5).

COVID-19 vaccination offers significant protection against the virus(6). Unfortunately, vaccine allocation during the first 6 months of distribution demonstrated similar disparities to both disease incidence and outcomes among the general US adult population. CDC data show that Black adults received proportionally fewer first doses of COVID-19 vaccine than their non-Hispanic White counterparts during the initial phase of the vaccine roll out(7). As of June 15th, 2021, initial vaccinations were received by 8.8% of US adults who identified as Black despite their making up 12.4% of the total US adult population. Disparities were less evident in Hispanic populations, with 17.2% of vaccinated adults identified as Hispanic while accounting for 17.6% of the total population. In comparison, 61.2% of vaccinated adults were White despite making up 59.4% of the total adult population. This inequity is hypothesized to arise from ongoing structural racism fomenting barriers to healthcare and potentially greater vaccine hesitancy among people of color, (8) but is not insurmountable. In a national study of older adults (age 65+) receiving vaccinations through the VA during the first two months of the COVID-19 vaccine campaign (Dec 15, 2020 – Feb 23, 2020), vaccination was more likely among individuals who identified as Black, Hispanic, or AA/PI compared with those who identified as White (9).

Rural communities represent another vulnerable group experiencing higher rates of COVID-19 infection, hospitalization, and death throughout the pandemic. Among Veterans living with chronic viruses like HIV in rural areas, for example, entry into care is often delayed(10). Greater rurality was associated with a higher likelihood of poor health outcomes among patients infected with COVID-19 and lower likelihood of receiving the vaccine based on CDC data at the county level (11). In addition, rural residents were more likely to have to travel to non-adjacent counties to receive a vaccine. Rurality, therefore, may be a potent barrier to initial vaccine uptake and require greater efforts for rural residents to obtain vaccination (11).

Distribution of the COVID-19 vaccine in the US was a coordinated but complex effort. While the federal government was tasked with approving the three widely circulated vaccines, they were allocated on a weekly basis to each state and territory with distribution then determined by individual jurisdictions. As a result of vaccine scarcity, state and local vaccine availability was inconsistent during the first months of vaccine allocation(12).

In contrast, the VA provides care to over 9 million Veterans across nearly 1,300 sites in every state in the US; it is the largest single healthcare system in the US with relatively broad outreach and includes the Office of Rural Health. These and other programs in the VA may mitigate disparities by improving access to care. We hypothesized that RE disparities in initial COVID-19 vaccination would be mitigated in a national cohort of US Veterans, and that rurality would modify associations between RE and vaccination.

Methods:

Data: In this retrospective cohort study, we included demographic and clinical data for 5.8 million Veterans with a VA primary care visit during the 2019 calendar year (all age 18 and older). In order to receive care at the VA, it is necessary to be age 18 years and older to serve as an active-duty member of the Armed Forces. All data were obtained from the Corporate Data Warehouse (CDW). We identified individuals who received a first COVID-19 vaccine dose during the observation period (December 15th, 2020-June 15th, 2021). The CDW includes data for vaccine receipt both within the VA and non-VA facilities, although data is not available for Veterans who receive care through the Indian Health Service (IHS). Vaccination distribution at VA primarily followed the CDC phased allocation process, beginning on December 15, 2020(13), although age-based eligibility was broadened earlier and a COVID-19 vaccine was available to all Veterans by March 24th, 2021 (all US adults on April 19th, 2021)(14).

Primary Outcome: Initial COVID-19 vaccine receipt was the primary outcome and was ascertained, including non-VA vaccination as detailed above; VA uses a validated algorithm to identify COVID vaccination. Vaccination data are updated weekly and cleaned to eliminate duplicate entries(15). The VA immunization database includes data on COVID-19 vaccines administered at the VA as well as vaccines administered outside the VA using linked US national pharmacy databases and patient self-report recorded by VA providers. Using time-to-first-vaccination as the outcome, patients were censored with first COVID vaccination, death or end of the observation period, whichever came first as of June 15, 2021.

Predictors of Interest: Our predictors of interest were race/ethnicity (RE) and rurality. RE was self-reported in CDW and categorized into a single mutually exclusive group of non-Hispanic Black (Black), Hispanic, non-Hispanic White, Asian American/Pacific Islander (AA/PI), American Indian/Alaskan Native (AI/AN), Mixed (for individuals who self-identified as multiple races/ethnicities) and Other (included "Declined to answer" and "Unknown by patient" and missing)(16). Due to the unknown nature and potential heterogeneity of the "Other" RE group, we excluded the "Other" group for modeling purposes (17).

Rurality was based on 2019 home address at the zip code level and defined as urban, rural, and highly-rural based on Rural-Urban Commuting Area (RUCA) codes, where an area is defined as rural if it contains fewer than 35 people per square mile (18). We folded highly-rural into the rural category because it contained extremely few residents.

Other Covariates: We included covariates that were likely to contribute to vaccine uptake. Smoking status was ascertained using Health Factors Data(19); cigarette smoking Health Factors Data are used nationally by the VA Healthcare system and responses are categorized as current, former, or never smoker based on self-report. We used most frequent response to define the variable at the patient-level(19). To adjust for comorbidities, we used baseline Charlson Comorbidity Index (CCI) at the time of enrollment in the study during their primary care visit in calendar year 2019 (20) (comorbidities determined by at least one inpatient or two outpatient ICD codes for the conditions prior to baseline and CCI categorized as 0, 1, 2, and ≥3) (21). As a proxy for overall receptivity to vaccinations, influenza vaccination uptake during the 2019-2020 influenza season was determined using individual patient vaccination data in the electronic health record(22). We also included level of service connectedness as a means of determining disability compensation from active duty in the Armed Forces (none, <50% or ≥50%). Other covariates included age (in years; as a continuous variable), sex, and geographic region (North Atlantic, Southeast, Midwest, Pacific, Continental).

Statistical Analysis: We used descriptive statistics to measure central tendency for continuous variables and chi-square for categorical variables. For continuous variables we used t-test and for non-normal variables we used the Wilcoxon rank-sum. We used a Cox proportional hazards model to evaluate associations between RE and rurality groups and time to receipt of initial COVID-19 vaccine dose over 6 months. The start of follow-up (or time zero) was defined as the first date of COVID-19 vaccine becoming available in the US, namely December 15, 2020. Veterans were followed until receiving the 1st COVID vaccination dose, death, or reaching the end of 6-months without vaccination, whichever came first. Adjusted Hazard Ratios (HR) were estimated after accounting for age, sex, smoking status, CCI, prior influenza vaccination and service connectedness and geographic region, with the use of robust variance estimators to account for potential within-facility clustering. Because of a significant interaction between RE and rurality ($p<0.05$), a composite variable accounting for RE by rurality interactions was included in the final multivariable models to allow for direct comparisons across RE and rurality combinations with non-Hispanic White Urban patients as the reference group.

Sensitivity analyses: Because we suspected that prior vaccine behavior was important, we conducted Cox models by prior influenza vaccination status. In addition, separate models by sex were performed to determine whether the direction and strength of associations with RE and rurality persisted in women only. Finally, we conducted Cox Models including the "Other" RE category in the models.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). Proportional hazards assumptions were checked using cumulative martingale residuals and Kolmogorov-Type Supremum Tests. Statistical significance for hypothesis testing was based on a two-sided p value < 0.05.

Results:

Our study population included 5,871,438 Veterans (9.4% women), of whom 55.2% received at least one dose of a COVID-19 vaccine. We excluded a group that we categorized as 'Other' and composed 5.7% of the study population for whom RE was missing(17). Among this group were patients who declined to answer the question about RE identity (n=109,966, 1.9%), did not know their RE identity (n=38,804; 0.7%), or their RE was truly missing (n=182,191; 3.2%).

Vaccinated Veterans were older (mean age in years=66.3 (standard deviation (SD)=14.4 vs. unvaccinated=57.7 (18.0) p<0.001). The majority of Veterans were White (66.7%) and vaccinated Veterans were more likely to self-identify as Black (Vaccinated=18.2% vs. Unvaccinated=16.1% p<0.001). Vaccinated Veterans were less likely to reside in rural settings (Vaccinated=30.9% vs. Unvaccinated=35.7% p<0.001). Vaccinated Veterans had greater comorbidity burden, represented by higher CCI, compared with unvaccinated Veterans (Table 1).

Adjusted models determined that Black, Hispanic, and AA/PI individuals were more likely to receive a vaccination relative to White individuals, whereas AI/AN Veterans had decreased likelihood of vaccination regardless of rurality. Rural residence was associated with lower likelihood of receiving at least one dose of vaccine (Hazard Ratio=0.80 [Confidence Interval (CI) 0.80-0.81]).

In the final models including interactions between RE*rurality, urban Black individuals were 12% more likely to get vaccinated relative to urban White individuals; in addition, the only rural RE group more likely to be vaccinated than urban White individuals were rural Black Veterans (Urban Black HR=1.12 [CI 1.12-1.13], Rural Black HR=1.06 [1.05-1.06],) (Table 2, Figure 2). Other groups varied by RE and rurality compared with Urban White (Rural White HR=0.78 [0.78-0.79]; Rural Hispanic HR 0.98 [0.97-0.99] whereas Urban Hispanic HR=1.17 [1.16-1.18]); among AA/PI and mixed individuals, urban veterans were more likely to receive first vaccination but rural veterans were less likely to receive first COVID vaccination (Rural AA/PI HR=0.86 [0.84-0.88], Urban AA/PI HR=1.22 [1.21-1.23]; Rural Mixed HR=0.77 [0.75-0.79], Urban Mixed HR=1.05 [1.03-1.06]). AI/AN individuals were less likely to receive the first dose of vaccine compared to White counterparts, regardless of rurality (Rural AI/AN HR=0.76 [0.74-0.78], Urban HR=0.93 [0.91-0.95]).

Other covariates associated with vaccination included increasing age (HR=1.03 [1.03-1.03]), female sex (HR=1.05 [1.05-1.06]), greater disease burden compared with CCI=0 (CCI=1 HR=1.18 [1.17-1.18]; CCI=2 HR=1.22 [1.21-1.22]; CCI ≥3 HR=1.30 [1.29-1.30]), prior influenza vaccination (HR= 2.13 [2.12-2.13]) and geographic region compared to North Atlantic (Midwest HR=1.02 [1.01-1.03], Southeast HR=1.00 [0.99-1.00], Pacific HR=1.04 [1.04-1.04], Continental HR=0.92 [0.91-0.92])(Table 2).

In sensitivity analyses stratified by influenza vaccination, similar associations were observed for RE and COVID vaccination regardless of influenza vaccination during the preceding influenza season except for rural Black prior flu vaccinated individuals who had similar HR to urban White prior flu vaccinated individuals [1.01 (1.00-1.02], (Table 3). Separate models stratified by sex similarly found consistent associations, although the effects of RE and rurality were attenuated in women with rural Black women having similar HR to urban White women [0.99-(0.97-1.01)] (Table 3).

Finally, in sensitivity analyses including the "Other" RE category, the primary associations did not change; Veterans included in the Other category were less likely to be vaccinated (Urban-Other OR=0.67 [0.66-0.67] Rural-Other OR=0.83 [0.83-0.84]; (Appendix 1).

Discussion:

Whereas vaccination disparities have been prevalent in non-White populations in the general US population, Black, Hispanic, and AA/PI Veterans receiving care within VA were more likely to receive a COVID-19 vaccine during the first 6 months of the vaccination campaign. Of note, our observation period extends to the time when vaccinations were available to all US adults.

Our findings build on a recent study among those receiving care in VA examining disparities in vaccination uptake through February 23, 2021; before the vaccine was available to all US adults and all Veterans. Similar to our results, their investigation found that Black, Hispanic, and AA/PI veterans were more likely to receive a COVID-19 vaccine while AI/AN patients were less likely. The authors concluded that the VA's proactive vaccine distribution strategy may have mitigated disparities (9). For context, as vaccine supply increased nationally, RE disparities in vaccination status in the US decreased after the first 6 months, although were not eliminated(1). Our work adds to these initial observations by examining RE differences by urban compared with rural settings and finding that vaccination disparities are most prominent in rural settings in all RE except for Black-rural veterans.

There are likely several reasons why the VA successfully mitigated disparities during the initial phase of vaccine allocation. Proposed strategies for health equity have focused on a combination of factors: building trust, engaging local leaders, and eliminating barriers to care(23, 24). We speculate that the VA addressed these key components with a centralized, coordinated, national campaign deployed by locally engaged facilities with trusted primary care providers. This coordinated effort included active outreach to Veterans once they were eligible for the COVID-19 vaccine and expanding services to include weekend vaccination clinics (25). The VA's ability to track vaccine uptake for millions of patients and contact those who had not received a vaccine with information both about the vaccine and logistics for getting one, may have led to more equitable and rapid outreach to patients of color. This is in contrast to the non-Veteran population, which relied on state and local governments to distribute vaccines to hospitals and healthcare facilities, which have historically been less accessible to communities of color due to decades of under-investment in their healthcare(26).

It is possible that Veterans, regardless of RE, are less likely to experience vaccine hesitancy. Early data, as noted by the Secretary of Veterans Affairs, Denis McDonough, showed less vaccine hesitancy among Veterans of color than among Black US adults in the general population(27). Due to an established relationship, Veterans of all RE may be more likely to trust both their specific VA physician and the VA as a whole(27, 28). The observation that Veterans are less hesitant about receiving vaccines may also be due to vaccination requirements for service in the Armed Forces. While improved access to care and vaccine information were likely contributors to improved vaccine uptake among Veterans of color, vaccine hesitancy among communities of color may contribute to national disparities in vaccine receipt. Multiple studies have shown that even when there is ample availability of vaccines, Black and Hispanic US adults are less likely to obtain a vaccine due to greater hesitancy(29-31). This hesitancy may stem from decades of systemic racism within the healthcare system(32, 33), and may be mitigated with effective community engagement and trusted allies in healthcare.

There are several factors that are hypothesized to contribute to the higher rate of vaccination among AA/PI Veterans and in the US adult population as a whole. Multiple surveys have estimated vaccine hesitancy within AA/PI to be approximately 25%, which is lower than other RE groups(34). The observed higher relative rate of vaccination may be partially explained by a relatively large proportion of the AA/PI community working in healthcare with exposure to patients who were ill with the COVID-19 virus. In addition, language concordant information on vaccines was widely available for AA/PI individuals due to efforts by community organizers(35).

The lower relative rates of vaccination among AI/AN Veterans in our study is discordant with national data. Contrary to initial concerns about vaccine hesitancy among AI/AN adults, as a group, they have been vaccinated at higher rates than their White counterparts due to proactive distribution of vaccines by the IHS(36, 37). Overall, CDC data show that AI/AN US adults have received COVID-19 vaccines at a higher rate than the general US population(7). Many members of the AI/AN community who live in rural settings receive their care through the IHS. If AI/AN Veterans received their vaccine through the IHS, those data may not be captured in our outcome ascertainment, which may explain the differences in our findings.

Rurality is an often-recognized barrier to equitable healthcare. In our study, overall vaccinations in rural communities were lower compared with urban areas. This observation is likely due to challenges accessing care in the setting of greater distances traveled for vaccine administration. Similar disparities have been reported for preventive care such as lung cancer screening(38). CDC data showed that rural residents more often had to travel beyond adjacent counties to receive a vaccine, and that rural residents who infrequently traveled outside of their home county were less likely to be vaccinated. Barriers to care among persons residing in rural areas are especially difficult to overcome for older US adults, as well as persons without health insurance or healthcare. Further, numerous polls have shown greater vaccine hesitancy in rural communities. A recent poll by the Kaiser Family Foundation showed that 21% of respondents from rural areas would ‘definitely not’ get a vaccine, compared with 10% among urban respondents(39). While the VA has an institutional goal to provide accessible healthcare to Veterans in rural settings, additional strategies and outreach may be necessary to overcome barriers to accessing healthcare within rural communities.

Unsurprisingly, prior influenza vaccination was most strongly associated with COVID-19 vaccination. In sensitivity analyses stratified by prior influenza vaccination, we found persistently higher likelihood for COVID vaccination in non-White veterans, regardless of prior influenza vaccine receipt.

There are several limitations to this study. First, our primary outcome was uptake of a single dose of vaccine over a relatively short 6-month period, rather than full vaccination series adherence and boosting; longer observation time may be especially relevant to examine vaccination disparities in younger age groups. Further, we did not determine SARS-CoV-2 infection rates prior to initial vaccination and how this might also influence likelihood for vaccination subsequently. We chose to examine the first phase of vaccination allocation, however, as it was more useful in determining disparities due to the greatest vaccine scarcity during the initial vaccine distribution phase; future work should examine how vaccination was also associated with prior SARS-CoV-2 infection, as well as rates of breakthrough infections among those vaccinated and boosted. In addition, our data may not include all Veterans who received vaccines outside of the VA system. It is possible that Veterans received a vaccine outside of the VA because they were increasingly available in their community. However, this is unlikely to have occurred differentially by race and ethnicity. Throughout the observation period the necessary criteria to qualify for receipt of a vaccine changed and the vaccine was not strictly available to all patients at the start of the observation period. Vaccine eligibility was fluid, however, from the first day of availability, where comorbid burden and employment status were frequent justifications for earlier vaccination in younger age groups. Also due to initial scare vaccine supply, staff avoided vaccine waste earlier on and offered vaccinations more liberally than an age-alone cut off. In the first 30 days of vaccination, 17% of vaccinations went to Veterans under 55. These factors made it difficult to model for changing vaccine eligibility which could have created an immortal time bias in our analysis. Finally, while there were fewer women than men in this investigation, we considered vaccination patterns stratified by sex and found overall similar, although attenuated, associations among women.

Efficient, equitable vaccine distribution is crucial to combating the COVID-19 pandemic and promoting public health. Our investigation may offer insights into how to improve vaccine uptake for our nation as a whole. As millions more vaccines are administered across the country, including boosters, more data are needed to determine if this pattern persists among Veterans and if there are ways to utilize these data to circumvent inequities in the general US adult population. Our data show that a proactive approach in a well-developed, primary care-focused healthcare system, reducing barriers, and addressing vaccine hesitancy may help improve vaccination rates among people of color. In addition, our data show that inequities between rural and urban residents persist despite eliminating some barriers to accessing care and vast outreach efforts. For the health and wellbeing of our country, it is essential to better understand how to effectively increase vaccination rates in Black and Hispanic communities, who have been disproportionately affected by the pandemic.

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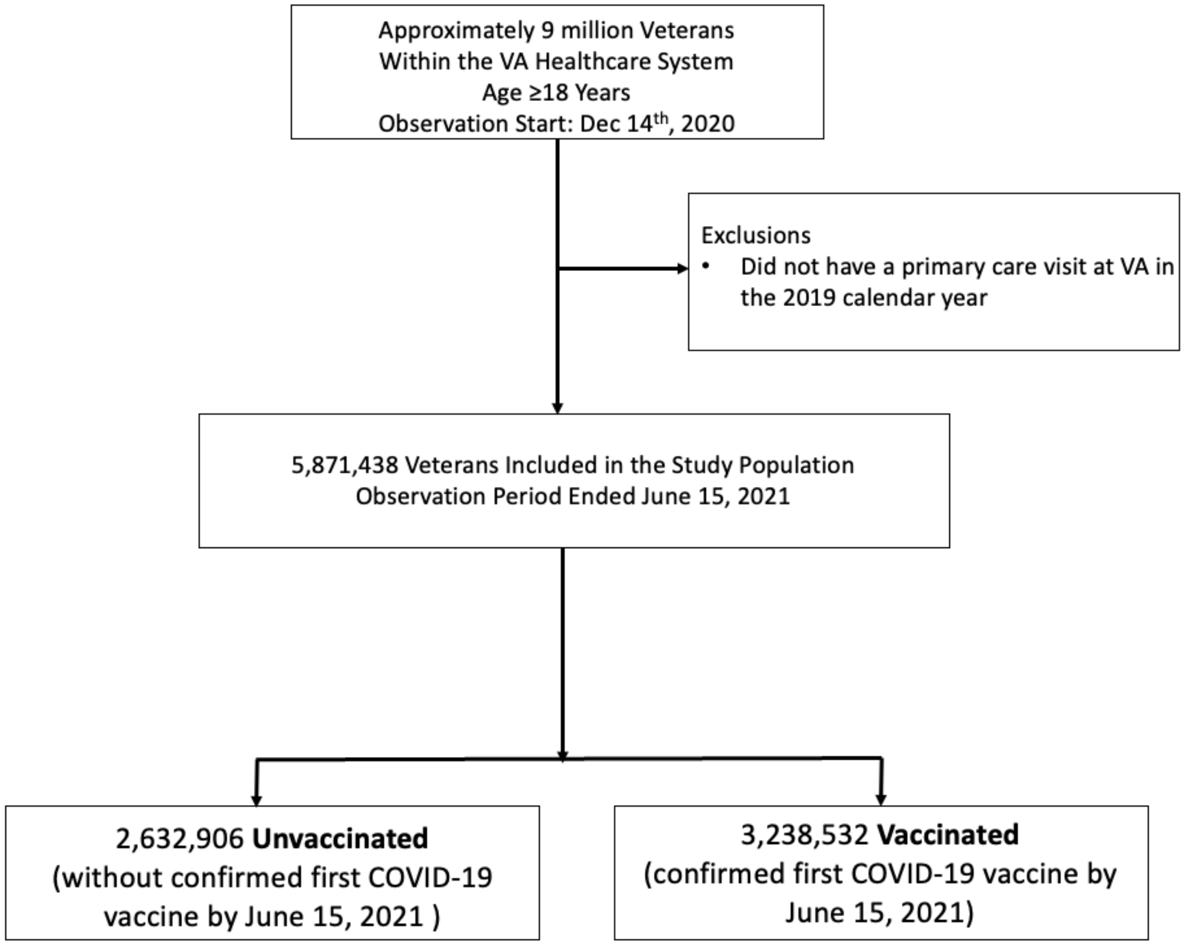
References

1. COVID-19 Weekly Cases and Deaths per 100,000 Population by Age, Race/Ethnicity, and Sex 2022 [Available from: https://covid.cdc.gov/covid-data-tracker/#health-equity-data.
2. Mackey K, Ayers CK, Kondo KK, Saha S, Advani SM, Young S, et al. Racial and Ethnic Disparities in COVID-19-Related Infections, Hospitalizations, and Deaths : A Systematic Review. Ann Intern Med. 2021;174(3):362-73.
3. Mude W, Oguoma VM, Nyanhanda T, Mwanri L, Njue C. Racial disparities in COVID-19 pandemic cases, hospitalisations, and deaths: A systematic review and meta-analysis. J Glob Health. 2021;11:05015.
4. Rentsch CT. Patterns of COVID-19 Testing and Mortality by Race and Ethnicity Among United States Veterans: A Nationwide Cohort Study. PLOS Digital Health. 2020.
5. Petersen K. Mortality Disparities in Racial/Ethnic Minority Groups in the Veterans Health Administration: An Evidence Review and Map. American Journal of Public Health. 2018;March 2018.
6. Prevention CfDCa. COVID-19 Vaccines Work CDC.gov2021 [updated December 23, 2021. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/work.html.
7. Demographic Characteristics of People Receiving COVID-19 Vaccinations in the United States Centers for Disease Control and Prevention2022 [Available from: https://covid.cdc.gov/dovid-data-tracker/#vaccination-demographic.
8. Jimenez ME, Rivera-Nunez Z, Crabtree BF, Hill D, Pellerano MB, Devance D, et al. Black and Latinx Community Perspectives on COVID-19 Mitigation Behaviors, Testing, and Vaccines. JAMA Netw Open. 2021;4(7):e2117074.
9. Haderlein TP, Wong MS, Jones KT, Moy EM, Yuan AH, Washington DL. Racial/Ethnic Variation in Veterans Health Administration COVID-19 Vaccine Uptake. Am J Prev Med. 2021.
10. Ohl M, Lund B, Belperio PS, Goetz MB, Rimland D, Richardson K, et al. Rural residence and adoption of a novel HIV therapy in a national, equal-access healthcare system. AIDS Behav. 2013;17(1):250-9.

11. Patel B. Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Coutines- United States, December 14,2020-April 10, 2021 Centers for Disease Control and Prevention2021 [Available from: https://www.cdc.gov/mmwr/volumes/70/wr/mm7020e33.html.
12. Michaud J. Distributing a COVID-19 Vaccine Across the U.S. - A Look At Key Issues. Kaiser Family Foundation [Internet]. 2020 September 5th 2021. Available from: https://www.kff.org/report-section/distributing-a-covid-19-vaccine-across-the-u-s-a-look-at-key-issues-issue-brief/.
13. Dooling K. Phased Allocation of COVID-19 Vaccines. Centers for Disease Control and Prevention. 2020.
14. Remarks by President Biden Marking the 150 Millionth COVID-19 Vaccine Shot [press release]. White House Briefing Room, April 6th, 2021 2021.
15. Corporate Data Warehouse [cited 2022 February 24th]. Available from: https://www.hsrd.research.va.gov/for_researchers/cdw.cfm.
16. Ferguson JM, Justice AC, Osborne TF, Magid HSA, Purnell AL, Rentsch CT. Geographic and temporal variation in racial and ethnic disparities in SARS-CoV-2 positivity between February 2020 and August 2021 in the United States. Sci Rep. 2022;12(1):273.
17. Hernandez SE, Sylling PW, Mor MK, Fine MJ, Nelson KM, Wong ES, et al. Developing an Algorithm for Combining Race and Ethnicity Data Sources in the Veterans Health Administration. Mil Med. 2020;185(3-4):e495-e500.
18. Economic Research Service U.S. Department of Agriculture. In: Agriculture Do, editor. 2021.
19. McGinnis KA, Brandt CA, Skanderson M, Justice AC, Shahrir S, Butt AA, et al. Validating smoking data from the Veteran's Affairs Health Factors dataset, an electronic data source. Nicotine Tob Res. 2011;13(12):1233-9.
20. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol. 1994;47(11):1245-51.
21. Justice AC, McGinnis KA, Skanderson M, Chang CC, Gibert CL, Goetz MB, et al. Towards a combined prognostic index for survival in HIV infection: the role of 'non-HIV' biomarkers. HIV Med. 2010;11(2):143-51.
22. Leuchter RK, Jackson NJ, Mafi JN, Sarkisian CA. Association between Covid-19 Vaccination and Influenza Vaccination Rates. N Engl J Med. 2022;386(26):2531-2.
23. Balasuriya L, Santilli A, Morone J, Ainooson J, Roy B, Njoku A, et al. COVID-19 Vaccine Acceptance and Access Among Black and Latinx Communities. JAMA Netw Open. 2021;4(10):e2128575.
24. Bibbins-Domingo K. Taking Vaccine to Where the Virus Is - Equity and Effectiveness in Coronavirus Vaccinations. JAMA Health Forum. 2021;2(e210213).
25. VA Weekend Vaccine Clinic 2021 [Available from: https://www.va.gov/connecticut-health-care/events/covid-19-vaccine-booster-clinic/.
26. Gillispie-Bell V. The Contrast of Color: Why the Black Community Continues to Suffer Health Disparities. Obstetrics and Gynecology. 2021;137(2):220-4.
27. Wentling N. VA Seeing No Difference in Coronavirus Vaccine Reluctance Based on Race. Stars and Stripes Magazine. 2021.
28. Jasuja GK, Meterko M, Bradshaw LD, Carbonaro R, Clayman ML, LoBrutto L, et al. Attitudes and Intentions of US Veterans Regarding COVID-19 Vaccination. JAMA Netw Open. 2021;4(11):e2132548.

29. Khubchandani J, Macias Y. COVID-19 vaccination hesitancy in Hispanics and African-Americans: A review and recommendations for practice. Brain Behav Immun Health. 2021;15:100277.
30. Baack BN, Abad N, Yankey D, Kahn KE, Razzaghi H, Brookmeyer K, et al. COVID-19 Vaccination Coverage and Intent Among Adults Aged 18-39 Years - United States, March-May 2021. MMWR Morb Mortal Wkly Rep. 2021;70(25):928-33.
31. Kricorian K, Turner K. COVID-19 Vaccine Acceptance and Beliefs among Black and Hispanic Americans. PLoS One. 2021;16(8):e0256122.
32. Katz RV, Green BL, Kressin NR, Kegeles SS, Wang MQ, James SA, et al. The legacy of the Tuskegee Syphilis Study: assessing its impact on willingness to participate in biomedical studies. J Health Care Poor Underserved. 2008;19(4):1168-80.
33. Rusoja EA, Thomas BA. The COVID-19 pandemic, Black mistrust, and a path forward. EClinicalMedicine. 2021;35:100868.
34. Ta Park VM, Dougan M, Meyer OL, Nam B, Tzuang M, Park LG, et al. Vaccine willingness: Findings from the COVID-19 effects on the mental and physical health of Asian Americans & Pacific Islanders survey study (COMPASS). Prev Med Rep. 2021;23:101480.
35. Quach T, Ethoan LN, Liou J, Ponce NA. A Rapid Assessment of the Impact of COVID-19 on Asian Americans: Cross-sectional Survey Study. JMIR Public Health Surveill. 2021;7(6):e23976.
36. Hilla L. COVID-19 Vaccination Among American Indian and Alaska Native People. Kaiser Family Foundation. 2021.
37. Foxworth R, Redvers N, Moreno MA, Lopez-Carmen VA, Sanchez GR, Shultz JM. Covid-19 Vaccination in American Indians and Alaska Natives - Lessons from Effective Community Responses. N Engl J Med. 2021;385(26):2403-6.
38. Kunitomo Y, Bade B, Gunderson CG, Akgun KM, Brackett A, Cain H, et al. Racial Differences in Adherence to Lung Cancer Screening Follow-up: A Systematic Review and Meta-analysis. Chest. 2022;161(1):266-75.
39. Kirzinger A. Vaccine Hesitancy in Rural American. Kaiser Family Foundation. 2021.

Figure 1: Patient Selection



	Unvaccinated N=2,632,906	Vaccinated N=3,238,532	Total N = 5,871,438	P-value
Age in years, Mean (SD)	57.7 (18.0)	66.3 (14.4)	62.4 (16.7)	<.0001
Age Group (%)				<.0001
<45	29.7	10.6	19.1	
45-54	14.6	10.3	12.2	
55-64	16.8	18.5	17.8	
65-74	22.7	36.7	30.4	
75+	16.2	23.9	20.5	
Sex, N (%)				<.0001
Female	279,943 (10.6)	269,247 (8.3)	549,190 (9.4)	
Male	2,352,958 (89.4)	2,969,285 (91.7)	5,322,243 (90.6)	
Race and ethnicity(%)				
White	66.9	66.7	66.8	
Black	16.1	18.2	17.2	
Hispanic	6.6	7.0	6.9	
Asian/Pacific Islander	1.7	2.0	1.9	
American Indian/Alaskan Native	0.8	0.6	0.7	
Mixed	0.9	0.8	0.8	
Other (missing, Declined answer, unknown to patient)	7.0	4.7	5.7	
Urban vs. rural (%)				<.0001
Urban	62.8	68.0	65.7	
Rural	35.7	30.9	33.0	
Highly Rural	1.5	1.1	1.3	
Prior Influenza Vaccination (2019-2020 season), N (%)	30.0	62.0	47.9	<.0001
Charlson Comorbidity Index, Median (IQR)	0 [0-1]	1 [0-2]	0 [0-1]	<.0001
Charlson Comorbidity Index (%)				<.0001
0	67.2	46.8	56.0	
1	16.1	22.0	19.4	
2	6.8	11.2	9.2	
3+	9.9	20.0	15.4	
Geographic region				<0.0001
North Atlantic	21.0	22.5	21.8	

Midwest	20.8	20.9	20.9	
Southeast	20.6	21.2	20.9	
Pacific	17.6	18.4	18.1	
Continental	20.0	17.0	18.3	
Service connectedness				
None	36.1	36.2	36.2	
< 50%	23.2	22.6	22.9	
≥ 50%	40.7	41.2	40.9	

Table 1: Characteristics of the Study Population

N=5,478,830	Hazard Ratio	95% Confidence Interval
Female vs. Male	1.05	1.05-1.05
Prior Influenza Vaccination (2019-2020 season)	2.13	2.12-2.13
Charlson Comorbidity (ref=0)		
1	1.18	1.17-1.18
2	1.22	1.21-1.22
3 or greater	1.30	1.29-1.30
Urban (Ref = Urban White)		
Urban Black	1.12	1.12-1.13
Urban Hispanic	1.17	1.16-1.18
Urban Asian/Pacific Islander	1.22	1.21-1.23
Urban American Indian/Alaskan Native	0.93	0.91-0.95
Urban Mixed	1.05	1.03-1.06
Rural White	0.79	0.78-0.79
Rural Black	1.06	1.05-1.06
Rural Hispanic	0.98	0.97-0.99
Rural Asian/Pacific Islander	0.86	0.84-0.88
Rural American Indian/Alaskan Native	0.76	0.74-0.78
Rural Mixed	0.77	0.75-0.79
Age, years	1.03	1.03-1.03
Geographic region (ref=North Atlantic)		
Midwest	1.02	1.01-1.03
Southeast	1.00	0.99-1.00
Pacific	1.04	1.04-1.04
Continental	0.92	0.91-0.92
Service connected (ref=None)		
< 50%	1.13	1.13-1.14
≥ 50%	1.23	1.22-1.23

Table 2: Factors associated with Uptake of COVID-19 Vaccine during first 6 months of vaccine availability in VA (Dec 14, 2020-Jun 15, 2021), Cox model

	Influenza vaccination (2019-20 season)*		Sex**	
	Yes	No	Women	Men
Race and ethnicity and rurality				
Rural				
Black	1.01 (1.00-1.02)	1.12 (1.11-1.13)	0.99 (0.97-1.01)	1.06 (1.05-1.07)
Hispanic	0.97 (0.96-0.99)	0.98 (0.96-0.99)	0.91 (0.88-0.94)	0.98 (0.97-0.99)
AA/PI	0.85 (0.82-0.87)	0.88 (0.85-0.91)	0.85 (0.79-0.91)	0.86 (0.84-0.88)
AI/AN	0.80 (0.78-0.82)	0.71 (0.68-0.73)	0.72 (0.67-0.77)	0.76 (0.74-0.78)
Mixed	0.79 (0.78-0.81)	0.73 (0.70-0.76)	0.76 (0.70-0.82)	0.77 (0.75-0.79)
White	0.80 (0.80-0.81)	0.75 (0.74-0.75)	0.76 (0.75-0.76)	0.79 (0.78-0.79)
Urban				
Black	1.09 (1.08-1.09)	1.17 (1.16-1.17)	1.01(1.00-1.02)	1.14 (1.13-1.14)
Hispanic	1.12 (1.11-1.12)	1.25 (1.24-1.26)	1.09 (1.07-1.11)	1.18 (1.17-1.18)
AA/PI	1.15 (1.13-1.16)	1.36 (1.34-1.38)	1.13 (1.10-1.16)	1.23 (1.22-1.24)
AI/AN	0.94 (0.91-0.96)	0.92 (0.89-0.95)	0.93 (0.88-0.98)	0.92 (0.90-0.94)
Mixed	1.02 (1.00-1.04)	1.08 (1.05-1.10)	1.00 (0.97-1.04)	1.05 (1.03-1.07)

Table 3: Cox models stratified by relevant prior influenza vaccination and sex

* models also adjusted for age, sex, Charlson, geographic region, and % service connected

** models also adjusted for age, prior influenza vaccination, Charlson, geographic region, and service connected

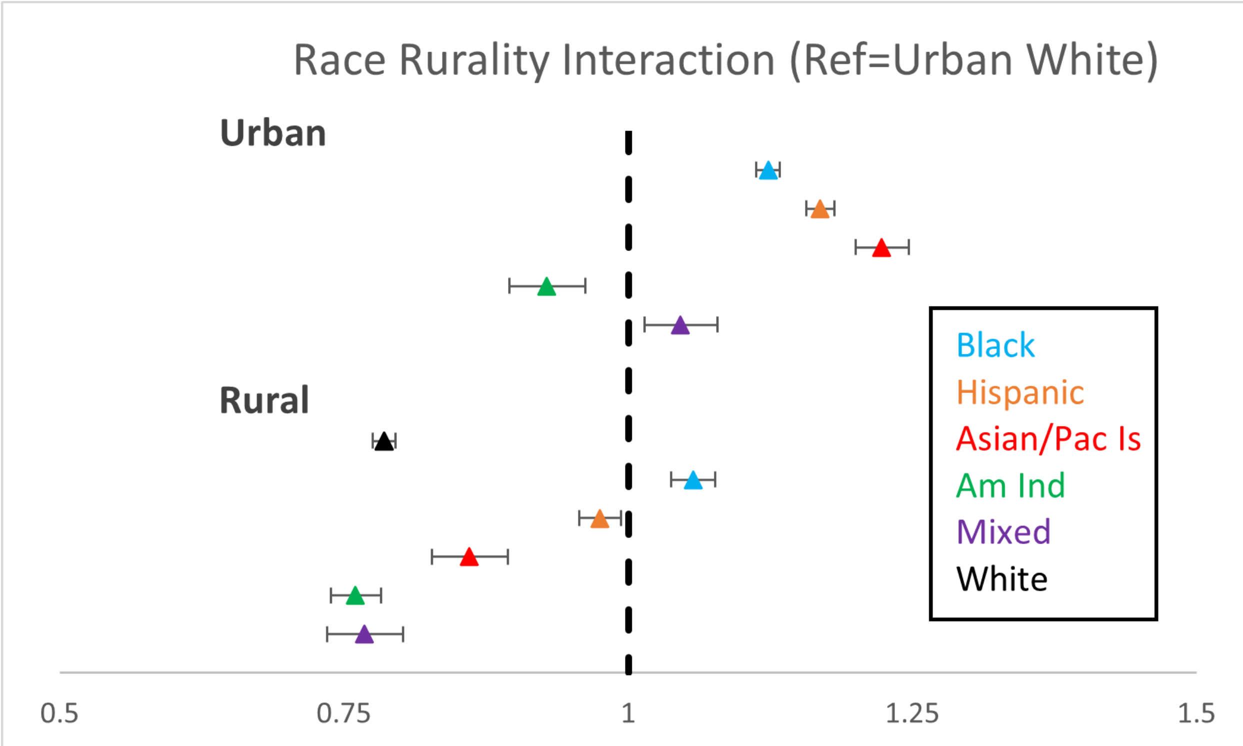


Figure 2. Forest plot of race and ethnicity interactions with rurality and associations with first COVID-19 vaccination among veterans
*Adjusted for age, sex, Charlson, geographic region, service connection, time-to-vaccination (in days) and prior influenza vaccination during 2020 influenza season.
Note: Asian/Pac Is=Asian American/Pacific Islander, Am Ind=American Indian/Alaskan Native

	Hazard Ratio	95% Confidence Interval
Female vs. Male	1.05	1.05-1.05
Prior Influenza Vaccination (2019-2020 season)	2.14	2.14-2.15
Charlson Comorbidity (ref=0)		
1	1.19	1.18-1.19
2	1.23	1.22-1.23
3 or greater	1.31	1.30-1.31
Urban (Ref = Urban White)		
Urban Black	1.12	1.12-1.13
Urban Hispanic	1.17	1.16-1.17
Urban Asian/Pacific Islander	1.22	1.21-1.23
Urban American Indian/Alaskan Native	0.93	0.91-0.94
Urban Mixed	1.04	1.03-1.06
Urban Other (missing, Declined to answer, unknown to patient)	0.67	0.66-0.67
Rural White	0.79	0.78-0.78
Rural Black	1.06	1.03-1.06
Rural Hispanic	0.97	0.91-0.94
Rural Asian/Pacific Islander	0.86	0.82-0.89
Rural American Indian/Alaskan Native	0.76	0.74-0.76
Rural Mixed	0.77	0.75-0.79
Rural Other (missing, Declined to answer, unknown to patient)	0.83	0.83-0.84
Age, years	1.03	1.03-1.03
Geographic region (ref=North Atlantic)		
Midwest	1.02	1.01-1.02
Southeast	1.00	1.00-1.00
Pacific	1.05	1.05-1.05
Continental	0.92	0.92-0.92
Service connected (ref=None)		
$< 50\%$	1.13	1.13-1.13
$\geq 50\%$	1.23	1.22-1.23

Appendix 1: Sensitivity analysis for factors associated with COVID-19 Vaccine including Other race/ethnicity category (Dec 14, 2020-Jun 15, 2021; n=5.7M)