Prevalence of SARS-COV-2 Vaccination and Factors Impacting Likelihood of Vaccination in a Nationwide Veterans Affairs Cohort of IBD Patients

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Lay Summary
Despite all efforts, about one-third of IBD patients are still not vaccinated. Although there is an emphasis on the booster dose, there is still a large population that has received no vaccination. Younger, healthy smokers with CD and on anti-TNF agents residing in the South and Midwest are less likely to get vaccinated. Targeted efforts should be made at this subset of IBD patients to increase vaccination rates.

Introduction
Inflammatory bowel disease (IBD), comprising ulcerative colitis (UC) and Crohn’s disease (CD), is a chronic inflammatory disorder of the gastrointestinal tract affecting over 3 million US adults. The incidence of SARS-COV-2 infection among patients with IBD is similar to that of the general population. However, within the IBD population, patients on steroids and vedolizumab have an increased risk of contracting SARS-COV-2, and steroids are associated with worse clinical outcomes related to Coronavirus disease 2019 (COVID-19). In response to this pandemic, FDA approved vaccines for prevention of SARS-COV-2 in the United States. These vaccines have been shown to be effective among patients with IBD and are widely available. However, only 71% of the US population 18 years or older have been fully vaccinated.

To the best of our knowledge, no studies have been done to evaluate the rates of SARS-COV-2 vaccination among the IBD population. Our aim was to determine the prevalence of SARS-COV-2 vaccination among a nationwide Veterans Affairs cohort of IBD patients and identify variables that may be associated with likelihood of vaccination. To achieve this goal, we used data from the Veterans Health Administration (VHA), the largest integrated health care system in the United States, serving up to 9 million veterans each year.

Methods
Study Design and Cohort
We performed a retrospective cohort study using a previously validated cohort of patients with IBD followed in the VHA. We identified all patients aged 18 years and older with IBD prior to December 18, 2020 (index date), the initiation date of COVID-19 vaccination in the VHA. Patients were followed through August 15, 2021. We obtained detailed demographic, comorbidity, baseline IBD medication data, and geographic region (West, Midwest, South, Northeast). The primary outcome of interest was receipt of vaccination.

Statistical Analysis
Descriptive statistics were compared between vaccinated (at least 1 dose) and unvaccinated individuals using Wilcoxon rank-sum (continuous variables) and χ² tests (categorical variables). To evaluate the distribution of vaccination over time, we produced histograms of first and second dose administration for each vaccine type. Kaplan-Meier failure curves were plotted to determine cumulative proportions of vaccination, both nationally and as stratified by geographic region. Comparisons were made using the log-rank test. Next, to identify risk factors associated with vaccination, we use multivariable logistic regression with backward stepwise selection to identify a candidate model. Multiple additional clinician-driven models were evaluated, and the final model was selected on the basis of a minimized Bayesian Information Criterion value. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Predicted probabilities of vaccination were then computed, and patient characteristics were summarized as stratified by low (<50%), medium (50% to 70%), and high (≥70%) predicted probabilities of vaccination. This project received Institutional Review Board approval from the Michael J. Crescenz Veterans Affairs Medical Center. All data management and analyses were performed using STATA 17.0/BE (College Station, TX).
Results
Cohort Characteristics and Vaccination Distribution
A total 14 450 patients with IBD were included. Patients receiving vaccination were older (median 71 vs 61 years, \(P < .001\)) and had more medical comorbidities (Supplemental Table 1, each comorbidity \(P < .001\)). Most patients had ulcerative colitis (61.9%) and were taking 5-aminosalicylic acid (5-ASA) alone (54.9%). In reference to the index date (December 18, 2020), cumulative vaccination nationwide reached 63.6% through August 15, 2021 (Figure 1A). There was significant geographic variation in vaccination, such that more patients received vaccination in the Northeast compared with the South (cumulative 67.8% vs 62.2%, \(P < .001\); Figure 1B). For both Pfizer and Moderna vaccines, the vast majority were administered in the first 3 months of the study window, with relatively few in the later follow-up period (Figures 1C/D). A total of 63.6% of the cohort received the first vaccination dose, and 61.8% received both primary vaccination doses.

Predicted Probability Categories of Remaining Unvaccinated
The final multivariable logistic regression model is shown in Supplemental Table 2. Compared with those with a high predicted probability of being vaccinated, patients with a low predicted probability were significantly younger (median 38 vs 75 years, \(P < .001\)), white or with Hispanic ethnicity (\(P < .001\)), current smokers (17.3% vs 11.5%, \(P < .001\)), less likely to have multiple comorbidities (each \(P < .001\)), and...
more likely to reside in the Southern United States (46.5% vs 35.4%, \(P < .001\); Table 1). Regarding IBD medication exposures, patients with high probability of vaccination were much more likely to be on 5-ASA alone (65.3% vs 33.6% low probability, \(P < .001\)), and patients with low probability of vaccination were much more likely to be taking antitumor necrosis factor (anti-TNF) agents alone (40.0% vs 10.0% high probability, \(P < .001\)).

Table 1. Patient characteristics as stratified by probability of COVID-19 vaccination.

| Factor                        | Predicted Probability of Receiving COVID-19 Vaccination | \(P\)  |
|-------------------------------|-------------------------------------------------------|-------|
|                               | \(<50\% (N = 2414)\) | \(50-70\% (N = 6644)\) | \(>70\% (N = 5392)\) |
| Age (years), median (IQR)     | 38 (33, 44)       | 65 (56, 72)       | 75 (71, 82)       | \(<0.001\) |
| Age Category                  |                         |                           |                           |          |
| <50 years                     | 2173 (90.0%)        | 718 (10.8%)        | 8 (0.1%)          | \(<0.001\) |
| 50-65 years                   | 241 (10.0%)         | 2550 (38.4%)       | 429 (8.0%)        |          |
| 65-80 years                   | 0 (0.0%)            | 3286 (49.5%)       | 3227 (59.8%)      |          |
| >80 years                     | 0 (0.0%)            | 90 (1.4%)          | 1728 (32.0%)      |          |
| Sex                           |                         |                           |                           | \(<0.001\) |
| Female                        | 203 (8.4%)           | 617 (9.3%)          | 314 (5.8%)        |          |
| Male                          | 2211 (91.6%)         | 6027 (90.7%)        | 5078 (94.2%)      |          |
| Race/Ethnicity                |                         |                           |                           | \(<0.001\) |
| White                         | 1954 (80.9%)         | 5434 (81.8%)        | 4224 (78.3%)      |          |
| Black                         | 146 (6.0%)           | 710 (10.7%)         | 856 (15.9%)       |          |
| Hispanic                      | 159 (6.6%)           | 231 (3.5%)          | 183 (3.4%)        |          |
| Other                         | 155 (6.4%)           | 269 (4.0%)          | 129 (2.4%)        |          |
| Current Smoker                | 417 (17.3%)          | 1091 (16.4%)        | 618 (11.5%)       | \(<0.001\) |
| Alcohol Abuse                 | 79 (3.3%)            | 247 (3.7%)          | 251 (4.7%)        | 0.005    |
| Drug Abuse                    | 73 (3.0%)            | 168 (2.5%)          | 111 (2.1%)        | 0.030    |
| IBD Type                      |                         |                           |                           | \(<0.001\) |
| Crohn’s Disease               | 1049 (43.5%)         | 2583 (38.9%)        | 1876 (34.8%)      |          |
| Ulcerative Colitis            | 1365 (56.5%)         | 4061 (61.1%)        | 3516 (65.2%)      |          |
| IBD Medication Group          |                         |                           |                           | \(<0.001\) |
| 5-ASA Alone                   | 811 (33.6%)          | 3596 (54.1%)        | 3522 (65.3%)      |          |
| TP alone                      | 250 (10.4%)          | 806 (12.1%)         | 494 (9.2%)        |          |
| Anti-TNF alone                | 966 (40.0%)          | 1346 (20.3%)        | 541 (10.0%)       |          |
| Anti-TNF + IM                 | 88 (3.6%)            | 262 (3.9%)          | 238 (4.4%)        |          |
| Vedolizumab                   | 191 (7.9%)           | 351 (5.3%)          | 417 (7.7%)        |          |
| Ustekinumab                   | 40 (1.7%)            | 82 (1.2%)           | 29 (0.5%)         |          |
| Tofacitinib                   | 26 (1.1%)            | 52 (0.8%)           | 30 (0.6%)         |          |
| Methotrexate alone            | 42 (1.7%)            | 149 (2.2%)          | 121 (2.2%)        |          |
| Steroid Use                   |                         |                           |                           | 0.97     |
| No Steroids                   | 2264 (93.8%)         | 6238 (93.9%)        | 5057 (93.8%)      |          |
| Steroids                      | 150 (6.2%)           | 406 (6.1%)          | 335 (6.2%)        |          |
| Obesity                       | 96 (4.0%)            | 608 (9.2%)          | 1020 (18.9%)      | \(<0.001\) |
| Hypertension                  | 176 (7.3%)           | 2930 (44.1%)        | 4267 (79.1%)      | \(<0.001\) |
| Diabetes Mellitus             | 38 (1.6%)            | 1140 (17.2%)        | 2391 (44.3%)      | \(<0.001\) |
| Arrhythmia                    | 51 (2.1%)            | 593 (8.9%)          | 1055 (19.6%)      | \(<0.001\) |
| Heart Failure                 | 6 (0.2%)             | 185 (2.8%)          | 462 (8.6%)        | \(<0.001\) |
| COPD                          | 70 (2.9%)            | 696 (10.5%)         | 1216 (22.6%)      | \(<0.001\) |
| Renal Failure                 | 16 (0.7%)            | 310 (4.7%)          | 647 (12.0%)       | \(<0.001\) |
| Metastatic Cancer             | 3 (0.1%)             | 28 (0.4%)           | 43 (0.8%)         | \(<0.001\) |
| US Region                     |                         |                           |                           | \(<0.001\) |
| West                          | 460 (19.1%)          | 1167 (17.6%)        | 1198 (22.2%)      |          |
| Midwest                       | 595 (24.6%)          | 1854 (27.9%)        | 1087 (20.2%)      |          |
| Northeast                     | 237 (9.8%)           | 727 (10.9%)         | 1199 (22.2%)      |          |
| South                         | 1122 (46.5%)         | 2896 (43.6%)        | 1908 (35.4%)      |          |

Abbreviation: COPD, chronic obstructive pulmonary disease.
Discussion

In this large VHA cohort of IBD patients, we found that only 61.8% of IBD patients were fully vaccinated. There were several factors that impacted the likelihood of getting vaccinated including age, race/ethnicity, and geographical location.

To the best of our knowledge, no nationally representative studies have evaluated the prevalence of SARS-COV-2 vaccination among the IBD population. Different surveys conducted among IBD patients from European countries and the United States reported vaccination intent between 50% to 81%. These match the actual vaccination rates seen in our study and are close to the national vaccination rates in the United States.

In addition to determining the prevalence of vaccination, we also investigated factors that may impact likelihood of vaccination. We found that age was an important predictor, and older patients had a higher probability of getting vaccinated. Veterans with comorbidities including obesity, hypertension, diabetes mellitus, arrhythmia, chronic obstructive pulmonary disease (COPD), and renal failure were more likely to get vaccinated. These findings suggest that vaccination efforts should be more targeted towards younger, healthier adults.

Data from Kaiser family foundation on state-wide COVID-19 vaccination rate by race and ethnicity demonstrated lower vaccination rates among Black adults in the United States despite mortality rates from COVID-19 being 1.9 times higher in this population.8 By contrast, in this VHA cohort we found that Black patients had a relatively higher probability of receiving vaccination. This key difference may be reflective of national VHA initiatives to broadly promote vaccination and mitigate disparities across race or ethnicity. Despite the fact that smoking has been associated with severe SARS-COV-2 infection and worse in-hospital outcomes, we found that smokers were less likely to get vaccinated. Other studies have also shown similar findings that current smokers are more likely to be undecided or unwilling to vaccinate against COVID-19.9 Another important determinant was geographical location, with people residing in the Southern states and the Midwest being less likely to get vaccinated. Our data are in accordance with CDC, and this regional differences in vaccination status persists even among patients with IBD.

We also found that characteristics specific to IBD patients also impacted vaccination status. Patients with UC were more likely to get vaccinated. Concerning medications, we found that patients who were on 5-ASA compounds were more likely to be vaccinated. Conversely, patients who were on anti-TNF agents were less likely to get vaccinated. These findings imply that patients who have a more severe disease necessitating the use of anti-TNF agents, contrary to expectations, are less likely to get vaccinated. This is despite studies showing that anti-TNF agents do not impact the efficacy of vaccination among IBD patients, although infliximab has been associated with an attenuated anti-SARS-COV-2 antibody response.10

While evaluating the timing of vaccination, we found that the highest rates of vaccinations were at the beginning when patients were prioritized by age and comorbidities. After the initial wave, the vaccination rates fell and plateaued despite being available to anyone who was interested (Figure 1). Despite media and government efforts, there was no significant increase in the prevalence of rates over time.

This study has important limitations, including possible misclassification of vaccination exposures. It is possible that patients may have obtained vaccinated outside the VHA, and our rates may be lower than the actual rates. However, this is unlikely because the VHA was among the first organizations with ample vaccine supply to start vaccinations and had a nationwide campaign. Vaccination status is monitored for every patient, and time updating change in status is recorded. We also limited our cohort to patients who were actively followed in the VHA, thus identifying patients who tend to receive their care primarily at the VHA. There are also inherent external validity limitations to the VHA database, given that it is predominantly composed of an older male population.

In conclusion, we found that despite all efforts, about one-third of IBD patients in the VHA are still not vaccinated. Multiple factors impact the likelihood of vaccination, and efforts should be targeted towards younger, healthier adults who smoke, reside in the South and Midwest, have CD, and are on an anti-TNF agents. This is especially important considering the current exponential increase in SARS-COV-2 infection rates.

Author Contributions

N.M. substantially contributed to the design of the article, statistical analysis, and interpreting the relevant literature. Y.S. contributed to interpreting the relevant literature and drafting of the manuscript. N.K. contributed to the concept and design of the article, as well as critical revision of the brief report for important intellectual content.

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Conflicts of Interest

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