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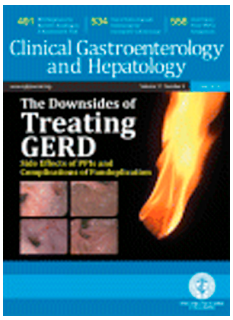

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COVID-19 vaccine is effective in inflammatory bowel disease patients and is not associated with disease exacerbation

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ABSTRACT

Background: Studies have shown decreased response to COVID-19 vaccinations in some populations. In addition, it is possible that vaccine-triggered immune activation could trigger immune-dysregulation and thus exacerbate inflammatory bowel diseases (IBD). In this population-based study we used the epi-Israeli IBD Research Nucleus (IIRN) validated cohort to explore the effectiveness of COVID-19 vaccination in IBD and to assess its effect on disease outcomes.

Methods: We included all IBD patients insured in two of the four Israeli health maintenance organizations (HMOs), covering 35% of the population. Patients receiving two Pfizer-BioNTech BNT162b2 vaccine doses between December 2020 to June 2021 were individually matched to non-IBD controls. To assess IBD outcomes, we matched vaccinated to unvaccinated IBD patients and response was analyzed per medical treatment.

Results: In total, 12,109 IBD patients received two vaccine doses, of whom 4,946 were matched to non-IBD controls (mean age 51±16 years and median follow-up 22 weeks (interquartile range [IQR], 4-24)). Fifteen patients in each group (0.3%) developed COVID-19 post vaccination (OR=1 [95%CI 0.49-2.05], *P*=1.0). Patients on tumor necrosis factor (TNF) inhibitors and/or corticosteroids did not have a higher incidence of infection. To explore IBD outcomes, 707 vaccinated IBD patients were compared to unvaccinated IBD patients by stringent matching (median follow-up, 14 weeks [IQR 2.3-20.4]). The risk of exacerbation was 29% in the vaccinated patients compared with 26% in unvaccinated patients (*P*=.3).

Conclusions: COVID-19 vaccine effectiveness in IBD patients is comparable to that in non-IBD controls and is not influenced by treatment with TNF inhibitors or corticosteroids. The IBD exacerbation rate did not differ between vaccinated and unvaccinated patients.

Keywords: SARS-CoV-2, vaccination, Crohn's disease, ulcerative colitis

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus has caused over 200 million confirmed cases of COVID-19 globally as of mid-2021 and more than 4.3 million deaths[1]. Mass vaccination is the most effective strategy for managing the pandemic. Various factors may interfere with host response to vaccination and potentially compromise vaccine effectiveness, including advanced age[2] and various types of immune suppression, such as immunosuppressive medications[3]. Indeed, decreased seroconversion rates to vaccines other than COVID-19 have been demonstrated in inflammatory bowel disease (IBD) patients treated with tumor necrosis factor (TNF) inhibitors[4-6]. Recent reports have suggested impaired serologic response to COVID-19 infection in patients treated with TNF inhibitors and immunomodulators[7]; serologic response to vaccination has also been found to be impaired[8,9]. However, as most of these patients do seroconvert[10,11] it is unclear whether this translates into higher infection rates [8,12,13]. Accordingly, concerns have been expressed as to whether the new COVID-19 vaccines are as effective in IBD patients, especially in those treated with immunosuppressive medications. One real-world study from Israel[14] and one prospective cohort study[9] have suggested similar effectiveness of the COVID-19 vaccine as in non-IBD subjects, but follow-up in these studies was short.

An additional concern is that immune activation due to COVID-19 vaccination would trigger IBD exacerbation. It is theoretically plausible that the immune activation initiated by COVID-19 vaccination might trigger IBD exacerbations through an immune-mediated dysregulation of the mucosal immune system. The effect of COVID-19 vaccination on IBD activity has only been assessed thus far for short follow-up periods (up to four weeks) [9,12]. For routinely administered vaccines other than COVID-19, no vaccine has yet been demonstrated to cause IBD flares, but there are no controlled studies specifically exploring their effect on disease outcomes in IBD.

In the present population-based controlled study, we aimed to explore both the effectiveness of COVID-19 vaccination in preventing SARS-CoV-2 infection, specifically in patients treated with TNF inhibitors and corticosteroids, and its effect on IBD course.

METHODS

For this study, we utilized the administrative database of the validated Israeli IBD Research Nucleus (epi-IIRN) cohort. The epi-IIRN includes all IBD patients in Israel, identified by validated case ascertainment algorithms, with three non-IBD controls (identified by the algorithms as not having IBD) matched to each patient based on age, sex, jurisdiction and Health Maintenance Organization (HMO). The previously published development and validation process of the case ascertainment algorithms to identify patients with IBD within the HMOs showed high accuracy (99% specificity, 89% sensitivity, 92% positive predictive value and 99% negative predictive value)[15,16].

We included subjects from two of the four national HMOs, covering 35% of the Israeli population. The HMOs are fully computerized and maintain electronic records on all health contacts, diagnoses (International Classification of Diseases, Ninth Revision), medications, laboratory test results, and utilization of other ambulatory health services, linked online to a central server since 2000-2003 (depending on the HMO). Medication data are accurate since the Israeli health care system provides the drugs via the HMOs while covering their costs. SARS-CoV-2 polymerase chain reaction (PCR) data are extremely accurate, as PCR results in Israel have been universally recorded in the HMO electronic health records since the start of the pandemic. During the COVID-19 pandemic, the Israeli Ministry of Health required central online daily registration of COVID-19 vaccination and SARS-CoV-2 PCR results – enabling highly accurate assessment of vaccination impact[17].

On December 11, 2020, the U.S. FDA issued an emergency use authorization for the Pfizer-BioNTech BNT162b2 COVID-19 vaccine. The vaccination program began in Israel toward the end of December, 2020, and by June, 2021 56% of Israeli residents had received two

vaccine doses[17]. The follow-up period for the present study was thus from Dec. 1, 2020, to June 30, 2021. During this period, the only available vaccine in Israel was the Pfizer-BioNtech BNT162b2 vaccine. The unparalleled rapidity of the Israeli vaccination campaign and use of only one vaccine brand, alongside the epi-IIRN validated national longitudinal IBD database, offers a unique opportunity to explore the effects of vaccination on a large IBD population-based cohort with exact matching.

A portion of our data was included in the previous study by Ben-Tov et al[14] on vaccine effectiveness in IBD patients. Here, we added a second HMO, utilized more stringent matching, lengthened the follow-up period, and most importantly, explored the novel question of whether the vaccine influences IBD activity.

COVID-19 vaccine effectiveness

For this analysis, we excluded subjects who had confirmed SARS-CoV-2 infection or positive serology at any time prior to the second vaccine, and those who had received only one vaccine dose. Each vaccinated IBD patient was individually matched to a vaccinated non-IBD subject using the following variables: year of birth, sex, jurisdiction of residence, HMO, and dates of the first vaccination with a caliper of ±3 days.

A biased higher or lower response to vaccination may be a result of a different background infection rate between individuals with and without IBD. In order to explore this potential bias, we individually matched each unvaccinated IBD patient to a non-IBD unvaccinated control by year of birth, sex, jurisdiction of residence, and HMO. Comorbidities that according to the U.S. Centers for Disease Control and Prevention (CDC) may impact COVID-19 severity (Supp. Material – Appendix A) were compared between the matched groups to ensure balanced distribution.

To assess the influence of immunosuppressive medications on vaccine effectiveness, we performed a sub-analysis using propensity score matching to compare the SARS-CoV-2 infection rate among IBD patients treated with TNF inhibitors alone (infliximab, adalimumab,

golimumab, certolizumab pegol), systemic corticosteroids alone or combined TNF inhibitors and steroids at the time of vaccination to: (i) all other IBD patients and to (ii) patients treated with other biologics or small molecules (vedolizumab, ustekinumab, tofacitinib). To calculate propensity scores for both comparisons, a logistic regression model was applied, and matching was performed using the nearest neighbor with a caliper of.1. Variables included in the propensity score model were: IBD subtype (Crohn's disease [CD]/ulcerative colitis [UC]), age at diagnosis, year of birth, sex, pre-existing conditions score, HMO, jurisdiction of residence and time of the first and second vaccines (with a caliper of ±3 days). As an additional exact matching variable designed to correct for disease severity, we formed severity sub-groups through hierarchical clustering machine-learning methods based on the patients' blood work (hemoglobin, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], albumin, platelets, white blood cell count [WBC]) performed during the preceding year (Supp. Table 1). These sub-groups categorize patients with heterogeneous available data in order to assist in accounting for disease severity.

IBD activity post-vaccination

In order to explore the impact of vaccination on IBD disease course, we matched vaccinated (two doses) to unvaccinated IBD patients by sex, jurisdiction of residence, IBD type (CD or UC), disease severity clusters based on blood work (as defined above), number of disease flares during the preceding two years (defined as any event of medication escalation, all-cause hospitalization, or steroid use), and age at IBD diagnosis (with a caliper of ± one year) (Supp. Table 1 and Appendix C). We excluded subjects who had confirmed SARS-CoV-2 infection or positive serology at any time prior to the second vaccine and, in matched controls, prior to the vaccinated date of the matched patient.

To further reduce the possibility of a confounding effect stemming from disease severity, the interval from the most recent flare to the first vaccine was used as an additional matching variable. The duration of follow-up of each IBD vaccinated-IBD unvaccinated pair was from

the date of the second vaccination of the case until the earliest of the following: vaccination date of the unvaccinated individual, SARS-CoV-2 positivity of any one of the pair, death or June 30, 2021. In the event that a control was vaccinated, he/she was converted to a case and was re-matched accordingly.

The outcome of IBD exacerbation was defined as treatment escalation, commencement of corticosteroids or enema, or hospitalization (Appendix C**). In addition, a sensitivity analysis was performed using a narrow definition of commencement of corticosteroids only.**

Statistics

Variables are presented as mean ± standard deviation or median (interquartile range) for continuous and categorical variables respectively. Comparisons between groups were made by Student's t-test, Wilcoxon rank sum test, one-way ANOVA and χ^2, as appropriate. Due to the large sample size, p-values are presented along with standardized mean differences (SMD), in which an SMD greater than.1 was considered meaningful. Odds ratios were calculated using the Haldane-Anscombe correction to express the association between the exposure (e.g. IBD patients vs. non-IBD patients) and the outcome (e.g. positive PCR test). Time to positive SARS-CoV-2 PCR test and to IBD flares are presented using Kaplan-Meier survival curves and compared using the log-rank test with robust variance estimator[18] to account for the individual matching. Analyses were performed using R; $p < .05$ was considered significant. The study was approved by the local ethics committee.

RESULTS

COVID-19 vaccine effectiveness

Between Dec. 1, 2020 and June 30, 2021, 12,109 IBD patients and 31,427 non-IBD controls without previous recorded SARS-CoV-2 infection received two vaccine doses (Figure 1). The cohort included 4,946 pairs, matched for year of birth, sex, jurisdiction of residence, HMO, and vaccination dates. The groups were well balanced, with SMD <.1 for all demographic and disease characteristic variables (Table 1, Supp. Figure 1). The post-vaccination SARS-CoV-2 infection rate was identical between vaccinated IBD patients (15/4,946 [0.3%]) and vaccinated non-IBD controls (15/4,946 [0.3%]; OR = 1 [95%CI 0.49-2.05], *P*=1.0) (Figure 2). Similarly, time to positive SARS-CoV-2 PCR showed no difference between the groups (Supp. Figure 2).

Effect of medical therapy on vaccine effectiveness

Of the 536 vaccinated IBD patients receiving TNF inhibitors and/or corticosteroids at the time of vaccination, 2 (0.4%) had a positive SARS-CoV-2 PCR during the study period, compared to 36/11,573 (0.3%) vaccinated IBD patients who did not receive these medications (*P*=1.0). Propensity score matching was successful for 502 pairs and showed similar infection rates (2/502 [0.4%] for TNF inhibitors/steroids vs. 0/502 for all others; *P*=.48; Figure 2).

In order to further reduce confounding, we compared patients on TNF inhibitors/corticosteroids to patients on any biologics other than TNF inhibitors in order to capture a group with likely greater disease severity, with similar results (2/536 [0.4%] for TNF inhibitors/steroids vs. 0/189 for all other biologics; *P*=.97; Figure 2). Finally, the latter groups were compared by propensity score after more stringent matching by a variety of IBD and demographic variables, including exact matching of IBD severity **(**Supp. Figure 3). The matched analysis compared 125 patients in each group; no patients from either group tested positive for SARS-CoV-2 (Figure 2).

Background SARS-CoV-2 infection rates in unvaccinated IBD patients and unvaccinated non-IBD controls

We considered the possibility that IBD patients may have exercised greater caution in their attempts to avoid exposure to SARS-CoV-2, thus decreasing the background infection rate compared to non-IBD subjects and confounding the estimate of vaccine effectiveness. Therefore, we determined the SARS-CoV-2 infection rate during the study period among 4,694 unvaccinated IBD patients matched to 4,694 unvaccinated non-IBD controls. Infection rates were slightly higher in the unvaccinated IBD patients (461/4,694 [9.8%]) than in the matched unvaccinated non-IBD individuals (362/4,694 [7.7%], OR = 1.3 [95%CI 1.13-1.51], *P*=.0003). The observed difference was in the opposite direction from the hypothesis and thus it does not confound the conclusion that the vaccine is at least as effective in the IBD population as in non-IBD controls.

Effect of vaccination on IBD disease activity

For this analysis, 2,108 vaccinated IBD patients were matched to unvaccinated IBD patients by sex, jurisdiction of residence, IBD type (CD or UC) and disease severity according to bloodwork clusters. Median follow-up was 12 weeks (IQR 2.4-20.6). No difference in disease outcome was seen during the first 40 days after the second vaccination, but thereafter, time-to flare was shorter in vaccinated compared to unvaccinated IBD patients (Supp. Figure 4). Overall, 44% of vaccinated and 34% of unvaccinated patients experienced an exacerbation or treatment escalation (p<.0001; number needed to harm [NNH] = 10).

Considering the possibility that despite the comprehensive matching the model was still unable to fully account for baseline disease severity, we applied more stringent matching criteria including number of exacerbations during the previous two years and time interval from the last exacerbation (defined as in the outcome). This cohort included 707 pairs of vaccinated and unvaccinated IBD patients with similar baseline characteristics (Table 2), and a median follow-up of 14 weeks (IQR 2.3-20.4). No substantive difference in disease

outcomes was found between the groups (Figure 3); the overall risk of exacerbation was 29% in vaccinated patients and 26% in unvaccinated patients (*P*=.3).

Finally, in light of the relatively high exacerbation rate, we performed a sensitivity analysis on the same cohort using a narrow definition of commencement of corticosteroids only. Here, too, no difference was found between the groups (Figure 4); the overall risk of exacerbation was 1.4% in vaccinated patients and 2.1% in unvaccinated patients (*P*=.3).

DISCUSSION

In this population-based study of all patients from two of the four national HMOs in Israel, we found that the overall COVID-19 vaccine effectiveness was similar between IBD patients and matched non-IBD controls. Focusing on medical therapy, we found that patients on TNF inhibitors and/or corticosteroids did not have a higher SARS-CoV-2 infection rate, even after precise matching for demographics, underlying diseases and IBD severity.

Our initial comparison revealed that vaccination was associated with increased risk of IBD exacerbation from 40 days and onward, despite exact matching of demographics, laboratory markers of disease severity and number of exacerbations in the preceding two years. However, when we included in the analysis the recentness of the last exacerbation prior to baseline, the difference was attenuated and was no longer significant. This underscores the challenge of accounting for disease severity in administrative databases and the importance of stringent matching of disease severity when assessing the influence of an exposure on disease course.

The effect of COVID-19 vaccination on short term (four weeks) IBD course was assessed by two groups, reporting no clinical and laboratory exacerbation compared to pre-vaccination baseline in a prospective cohort of 185 patients with IBD stratified according to treatment[9], and no increase in corticosteroid prescription one month after vaccination in a large retrospective cohort compared with a matched unvaccinated cohort[12]. However, accurate capture of IBD exacerbation in a retrospective study is challenging. Furthermore, ruling out an effect of vaccination on IBD activity likely requires more than a month of follow-up. Our data enabled a more comprehensive definition of exacerbation, including hospitalizations, treatment escalation, and commencement of corticosteroid or enema. The broad definition and the longer follow-up period (median, 14 weeks) enabled improved capture of IBD exacerbation. In order to address the possibility that our broad definition could have

potentially over-diagnosed exacerbation, we performed a sensitivity analysis defining exacerbation as steroid commencement only and still found no difference between the groups.

The finding that TNF inhibitors did not affect vaccine efficacy requires further discussion in light of existing literature showing decreased serological response in patients on TNF inhibitors for various vaccines including hepatitis A[4], hepatitis B[5] and influenza[6] vaccines.

Regarding response to COVID-19 vaccination in TNF inhibitor treated patients, data are conflicting. Dailey et al[19] found a robust response to two vaccine doses in a small prospective cohort, and all 33 vaccinated IBD patients in the study seroconverted. Khan et al found that BNT162b2 and Moderna mRNA-1273 vaccines were effective in a large retrospective cohort of IBD patients, irrespective of medications, but follow-up was brief and the study did not include non-IBD controls[20]. In contrast, in a large retrospective study (CLARITY IBD), Kennedy et al[8] found lower antibody levels in infliximab-treated patients compared to vedolizumab-treated patients, though patients in this study received only one vaccine dose (Pfizer-BioNTech BNT162b2 or Astra-Zeneca ChAdOx1). Edelman-Klapper et al[9] prospectively followed a group of 185 IBD patients after two doses of BNT162b2 vaccine and found that while all patients on anti-TNF medication seroconverted, antibody levels were significantly lower and neutralizing and inhibitory functions were similarly lower in this patient group. These studies raise concern for reduced durability of vaccine efficacy. Two recent serological studies, the PREVENT-COVID study and the CORALE-IBD study found that the large majority of IBD patients seroconverted, though levels in TNF-inhibitor patients were somewhat lower[10,11]. Our findings support the notion that while post-vaccine antibody levels and function are both reduced in anti-TNF-treated patients, they are nonetheless sufficient to protect from infection for at least a 22-week median follow-up period.

Our findings support those of the two previous studies that addressed real-world COVID-19 vaccine effectiveness for preventing infection in patients on anti-TNF medication; neither study found increased COVID-19 incidence in these patients. However, Hadi et al[12] did not

specify length of follow-up and Ben-Tov et al[14] followed the cohort for a median of 10 weeks. In the current study, we have shown that vaccine effectiveness in IBD patients on TNF inhibitors and corticosteroids continues to be unimpaired for up to 22 weeks.

The strengths of our study include a large population-based cohort, as well as rigorous individual and propensity score matching in order to reduce the inevitable confounders inherent in retrospective research using observational data. As COVID-19 prevalence fluctuated greatly during the study period, exact matching of vaccination date enabled the comparison of subject pairs during the same time period, with identical background COVID-19 prevalence. The large population of IBD patients who received the vaccine in a relatively short period enabled us to retain sufficient homogenous numbers for meaningful analyses even after stringent matching. Furthermore, all vaccinated individuals in the study received the same vaccine (BNT162b2), contributing to the uniformity of the comparison. Rigorous pre-vaccine disease adjustment allowed accurate detection of the vaccine effect on IBD activity and led to the likely conclusion that the vaccine is not associated with increased IBD exacerbations. Finally, the follow-up period enabled better capture of SARS-CoV-2 infections.

Our finding of higher COVID-19 incidence in unvaccinated IBD patients compared to unvaccinated individuals without IBD may stem from the fact that the IBD patients had a higher prevalence of a variety of underlying medical conditions than the non-IBD group – among both unvaccinated as well as vaccinated individuals (Supp. Table 2). This finding serves to increase certainty that the low infection rate in vaccinated IBD patients was not biased by a lower background rate, and strengthens the significance of our finding that the vaccine protected IBD patients equally as well as those without IBD.

The main limitations of the study relate to its retrospective analysis of data obtained from an administrative database. It is possible that some hidden confounding variables were still not properly addressed and that some of the data were biased by misclassification. Nonetheless,

case ascertainment of IBD in the epi-IIRN database is one of the most accurate globally and registration of medications and COVID-19-related data are very accurate by virtue of the function of the Israeli health care system. The low infection rates in vaccinated subjects limits our statistical power to prove equivalent effectiveness, but the fact that the infection rate was so low in a very large cohort clearly shows that the vaccine was highly effective in both groups, including those on anti-TNF therapy.

While the number of matched patients available for analysis was inevitably much lower than the number in the total cohort due to rigorous matching, comparison of the group that participated in the effectiveness analysis to the entire cohort revealed minimal differences in most demographic parameters (Supp. Table 4**)**.

In conclusion, we found that COVID-19 BNT162b2 vaccine was equally effective in IBD patients and in the non-IBD population, including those on TNF inhibitors and corticosteroids, and likely did not increase the risk of IBD exacerbation. The former finding supports previous short-term follow-up data. The present study is the first large controlled study to address the latter conclusion using a broad definition of exacerbation and provides further reassurance regarding safety of the COVID-19 vaccine in IBD patients.

LEGENDS to FIGURES

Figure 1. Included patients from the epi-IIRN cohort

Footnote

[1]Non-IBD controls were matched by age, sex, HMO and jurisdiction of residence

[2]Included individuals were vaccinated with two doses of Pfizer-BioNTech BNT126b2 from December 2020 to June 2021

Figure 2. SARS-CoV-2 infection rate in (a) vaccinated IBD patients vs. vaccinated non-IBD subjects; (b) vaccinated IBD patients treated with anti-TNF and/or corticosteroid vs. all other IBD patients; and (c) vaccinated IBD patients treated with anti-TNF and/or corticosteroid vs. other biologics

Figure 3. Time to exacerbation in vaccinated vs. unvaccinated IBD patients matched for disease severity, number of pre-vaccine flares and recentness of last flare

Figure 4. Time to steroid administration in vaccinated vs. unvaccinated IBD patients matched for disease severity, number of pre-vaccine flares and recentness of last flare

Supplementary Figure 1. Covariate balance for vaccinated IBD patients vs. vaccinated non-IBD subjects

Supplementary Figure 2. Survival curves for time to first positive PCR for IBD vs. non-IBD

Supplementary Figure 3. Covariate balance for vaccinated IBD patients on anti-TNF vs. other biologics

Supplementary Figure 4. Time to exacerbation in vaccinated vs. unvaccinated IBD patients matched for disease severity

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Table 1: Basic characteristics of vaccinated patients with and without IBD in the matched cohort (count (%), mean±SD or medians (IQR) are presented as appropriate)

	Non-IBD (n=4,946)	**IBD (n=4,946)**	**p-value**	**SMD**
Age	51±16	51±16	1	<0.001
<18	20 (0.4%)	20 (0.4%)		
18-39	1,288 (26%)	1,288 (26%)		
40-59	2,047 (41%)	2,047 (41%)		
60-69	823 (17%)	823 (17%)		
70-79	627 (13%)	627 (13%)		
80+	141 (3%)	141 (3%)		
Sex - Males	2,412 (49%)	2,412 (49%)	1	<0.001
Duration of follow-up after 2nd vaccine (weeks)	22 (4-24)	22 (4-24)	1	<0.001
IBD type				
CD	-	2,447 (49%)	-	-
UC	-	2,499 (51%)	-	-
Disease duration (years)	-	12 (1-24)	-	-
Treatment – during the preceding year				
5-ASA	-	1,441 (29%)	<0.001	0.91
corticosteroid	-	203 (4%)	<0.001	0.29
immunomodulator	-	294 (6%)	<0.001	0.36
anti-TNF	-	487 (10%)	<0.001	0.47
vedolizumab	-	185 (4%)	<0.001	0.28
ustekinumab	-	96 (2%)	<0.001	0.2
tofacitinib	-	28 (1%)	<0.001	0.11
IBD hospitalization – ever	-	2,329 (47%)	<0.001	1.33
IBD surgery – ever	-	668 (14%)	<0.001	0.56
Corticosteroids therapy – ever	-	2,722 (55%)	<0.001	1.57
Pre-existing conditions score[1]			0.011	0.073
0	2,099 (42%)	2,001 (41%)		
1	1,388 (28%)	1,352 (27%)		
2	696 (14%)	736 (15%)		
3	396 (8%)	404 (8%)		
≥4	367 (7%)	453 (9%)		

[1]Count of total number of pre-existing conditions defined by the CDC as risk factors (**Appendix A)**

IQR – interquartile ratio; **5-ASA** – 5-aminosalicylic acid (mesalamine); **TNF** – tumor necrosis factor

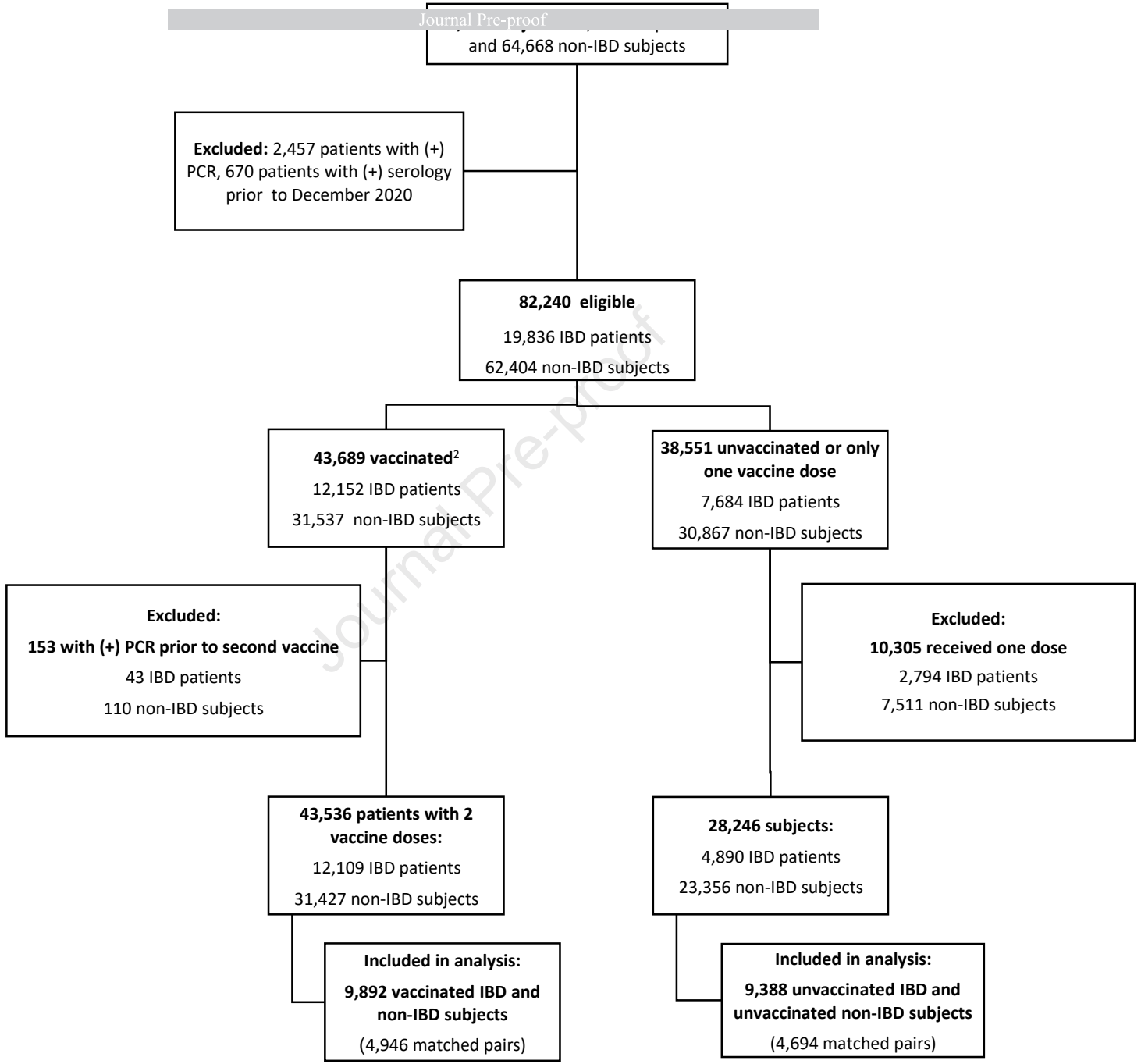
Table 2: Basic characteristics of vaccinated and unvaccinated IBD patients in the matched cohort (count (%), mean±SD or medians (IQR) are presented as appropriate)

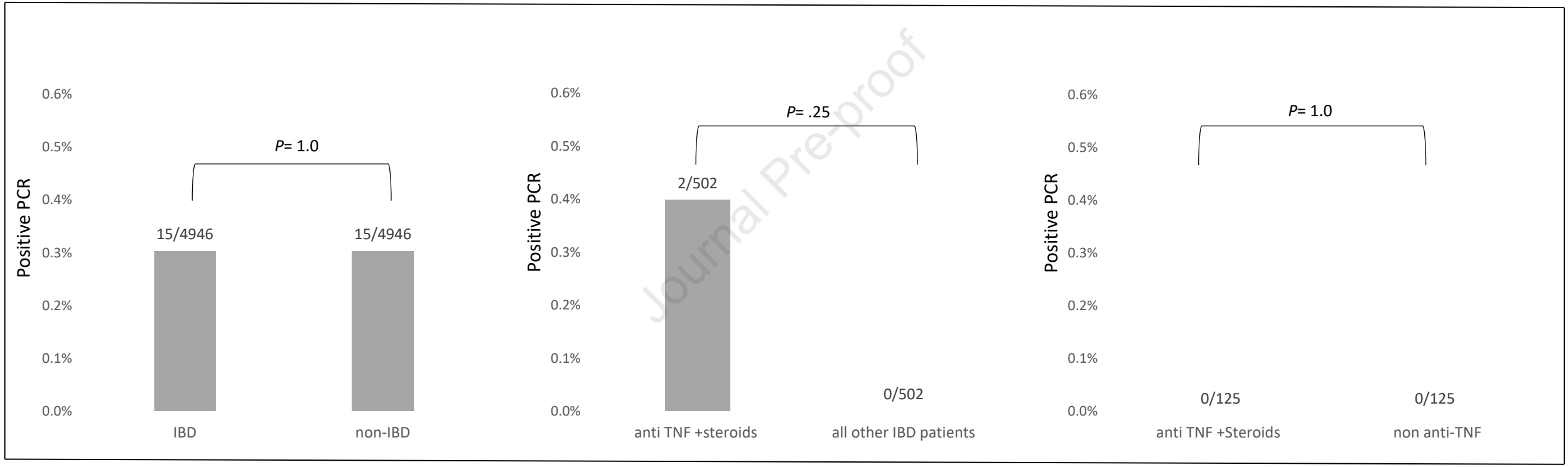
	Non-Vaccinated (n=707)	**Vaccinated (n=707)**	**p-value**	**SMD**
Age	31±13.0	31±13.0	1	<0.001
Sex - Males	358 (50.6%)	358 (50.6%)	1	<0.001
Duration of follow-up after 2nd vaccine (weeks)	14 (2.3-20.4)	14 (2.3-20.4)	1	<0.001
IBD type				
CD	485 (69%)	485 (69%)	1	1
UC	222 (31%)	222 (31%)	1	1
Disease duration (years)	8.6 (5.4-12)	8.6 (5.4-12)	1	<0.001
Treatment – over last year				
5-ASA	94 (13.3%)	114 (16.1%)	0.154	0.080
corticosteroid	23 (3.3%)	16 (2.3%)	0.330	0.060
immunomodulator	25 (3.5%)	35 (5.0%)	0.235	0.070
anti-TNF	95 (13.4%)	107 (15.1%)	0.403	0.049
vedolizumab	18 (2.5%)	30 (4.2%)	0.106	0.094
ustekinumab	8 (1.1%)	12 (1.7%)	0.499	0.048
tofacitinib	1 (0.1%)	2 (0.3%)	1.0	0.031
IBD hospitalization - ever	271 (38.3%)	304 (43.0%)	0.083	0.095
IBD surgery - ever	65 (9.2%)	94 (13.3%)	0.018	0.130
Corticosteroids therapy – ever	350 (49.5%)	376 (53.2%)	0.183	0.074
Disease activity group[1,2]			1	<0.001
1	76 (12%)	76 (12%)		
2	508 (83%)	508 (83%)		
3	32 (5.2%)	32 (5.2%)		

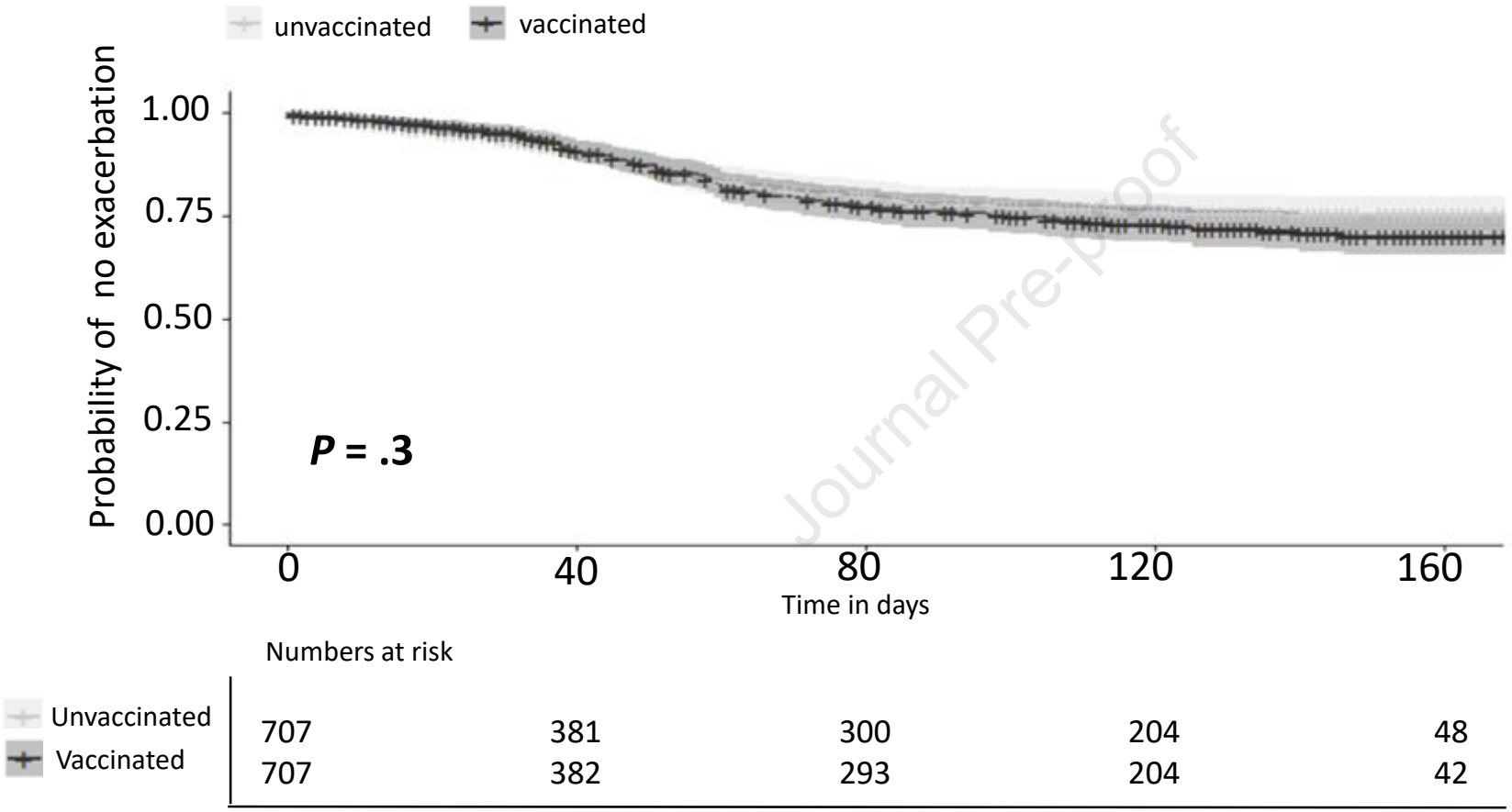
[1]Disease activity group calculated by hierarchical clustering of laboratory results **(Supp. Table 1, Appendix B)**

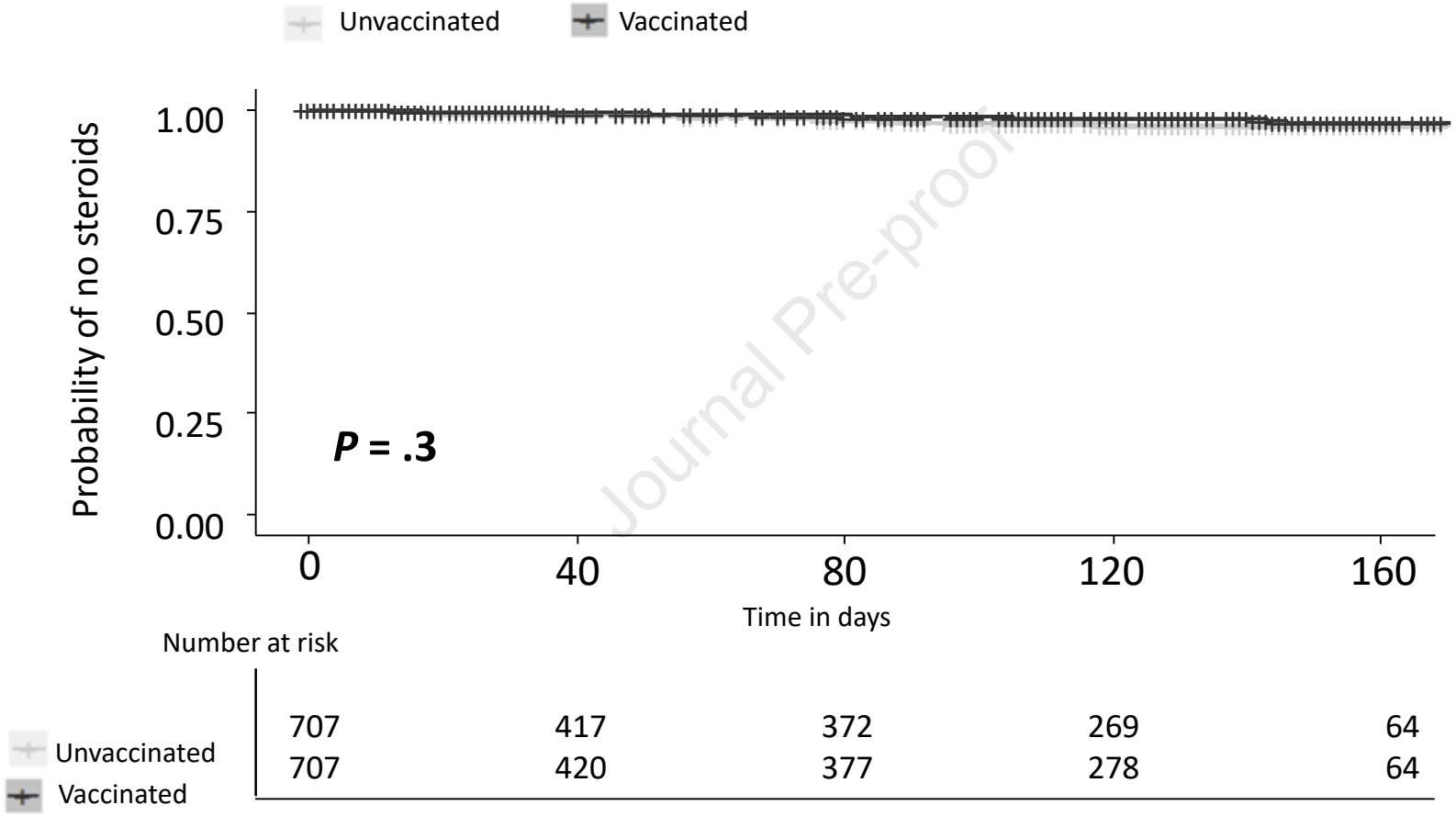
[2]91pairs had no laboratory results and could not be assigned to a disease activity group

5-ASA – 5-aminosalicylic acid; **TNF** – tumor necrosis factor









What you need to know

BACKGROUND

While Pfizer COVID-19 vaccine is extremely effective at preventing infection, questions have arisen regarding its effectiveness in inflammatory bowel disease (IBD) patients on immunosuppressive medications. Additionally, its effect on IBD outcomes has not been assessed.

FINDINGS

In a large population-based study, Pfizer COVID-19 vaccine was equally effective at preventing infection in IBD patients, including those on immunosuppressive medication, as in non-IBD subjects. Vaccinated IBD patients had no more disease exacerbations after vaccination than unvaccinated IBD patients.

IMPLICATIONS FOR PATIENT CARE

The study is the first to demonstrate that the Pfizer COVID-19 vaccine provided excellent protection for IBD patients on immunosuppression for as long as 22 weeks, and that no worsening of IBD outcomes occurred after vaccination.