




# Comparative Effectiveness of BNT162b2 and mRNA-1273 Vaccines Against COVID-19 Infection Among Patients With Systemic Autoimmune Rheumatic Diseases on Immunomodulatory Medications

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**ABSTRACT. Objective.** To compare the effectiveness of mRNA vaccines (BNT162b2 vs mRNA-1273) against coronavirus disease 2019 (COVID-19) infection among patients with systemic autoimmune rheumatic diseases (SARDs) on immunomodulatory medications.

**Methods.** We identified patients with SARDs being treated with disease-modifying antirheumatic drugs (DMARDs) and/or glucocorticoids in the Mass General Brigham healthcare system who received either BNT162b2 or mRNA-1273 as their initial vaccine series. Patients were followed until positive SARS-CoV-2 test, death, or February 22, 2022. We compared the risk of breakthrough infection between BNT162b2 and mRNA-1273 vaccine recipients using time-stratified, overlap propensity score (PS)-weighted Cox proportional hazard models.

**Results.** We identified 9838 patients with SARDs who received BNT162b2 or mRNA-1273. Demographic and clinical characteristics were similar in both groups after overlap weighting: mean age 61 years, 75% female, 52% with rheumatoid arthritis, 74% receiving conventional synthetic DMARDs, and 43% receiving biologic DMARDs. Of 5516 BNT162b2 and 4322 mRNA-1273 recipients, 446 and 329 had a breakthrough infection, respectively. The corresponding time-stratified PS-weighted rate difference of breakthrough infection was 0.71 (95% CI -0.70 to 2.12) per 1000 person-months with a weighted hazard ratio (HR) of 1.12 (95% CI 0.90 to 1.39). When follow-up was censored prior to the Omicron wave, there was a trend toward higher breakthrough risk with BNT162b2 vs mRNA-1273 (weighted HR 1.34, 95% CI 0.91 to 1.98).

**Conclusion.** Among patients with SARDs, the risk of breakthrough COVID-19 infection is similar after receiving either BNT162b2 or mRNA-1273. Patients with SARDs initiating the vaccine series should be encouraged to receive whichever mRNA vaccine is available.

*Key Indexing Terms:* epidemiology, infection, vaccines

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Patients with systemic autoimmune rheumatic diseases (SARDs) who use immunomodulatory treatments are at increased risk for severe coronavirus disease 2019 (COVID-19).<sup>1,2</sup> SARS-CoV-2 vaccines reduce the risk of COVID-19 and severe outcomes in the immunocompetent and immunosuppressed populations.<sup>3,4</sup> However, many immunomodulator users have a blunted immune response to vaccination and are at increased risk for breakthrough infection compared to immunocompetent individuals.<sup>5,7</sup> In this context, studies have demonstrated that the response to vaccination in immunomodulator users can be improved by temporarily holding immunomodulators and by administering additional vaccine doses.<sup>6</sup> Little is known, however, regarding the comparative effectiveness of vaccines on the risk of breakthrough infection among immunomodulator users and whether one vaccine may be preferred.

A previous study found that the mRNA-1273 (Moderna) vaccine may have greater effectiveness against breakthrough infection when compared with BNT162b2 (Pfizer-BioNTech) in the population of Veterans Affairs (VA) beneficiaries.<sup>8</sup> More recently, a large study of immunomodulator users found that those who received mRNA-1273 had a greater humoral immunologic response than those who received BNT162b2.<sup>9</sup> Little is known, however, regarding other potential differences in the immunologic response to mRNA-1273 or BNT162b2 in SARDs that may affect efficacy against clinical outcomes. Additionally, studies have suggested that recipients of mRNA-1273 vs BNT162b2 with a history of rheumatic disease had a lower risk of breakthrough infection but were susceptible to important sources of confounding, including the timing of vaccination.<sup>3,10</sup>

The objective of the current study is to assess the comparative effectiveness of BNT162b2 vs mRNA-1273 on the risk of breakthrough infection among patients with SARDs using immunomodulators.

## METHODS

*Study design, data source, and study population.* In this observational cohort study, we compared the risk of COVID-19 breakthrough infection in individuals with SARDs on immunomodulatory medications who received BNT162b2 to those who received the mRNA-1273 vaccine. Patients with a diagnosis of a SARD who received either a BNT162b2 or mRNA-1273 vaccine were identified from the Mass General Brigham (MGB) Enterprise Data Warehouse (EDW). MGB is a multicenter healthcare system that includes a total of 14 hospitals, including 2 tertiary care hospitals (Massachusetts General Hospital and Brigham and Women's Hospital), as well as other primary care and specialty outpatient centers in the greater Boston, Massachusetts area. This study was approved by the MGB Institutional Review Board (2020P000833). Patient consent was not required for this project as it was deemed Health/Medical Records research and did not meet the definition of Human Interaction/Intervention research.

We identified patients aged  $\geq 18$  years who were Massachusetts residents and received a BNT162b2 or mRNA-1273 vaccine dose between the date they were made available and February 2, 2022. We limited our study population to Massachusetts residents (as obtained by primary address in the electronic health record [EHR]) because vaccination data from the Massachusetts state database was populated in the EHR and all immunizations administered in Massachusetts are required by law to be reported to the Massachusetts Immunization Information System.<sup>11</sup> The index date was the date of the first mRNA vaccine administration.

From this population, we included patients if they had (1) at least 2 instances of a rheumatic disease International Classification of Diseases, 9th revision (ICD-9) or 10th revision (ICD-10) code within 2 years of the index date (one within the previous 12 months); and (2) a conventional synthetic (cs-), biologic (b-), or targeted synthetic (ts-) disease-modifying antirheumatic drug (DMARD), prescription/administration within 12 months of the index date, and/or (3) a prescription for a minimum of 30 pills of either prednisone or methylprednisolone within 6 months of the index date (Supplementary Materials, available with the online version of this article). The positive predictive value (PPV) for a similar rules-based algorithm to identify rheumatoid arthritis (RA) was 86%.<sup>12</sup> We reviewed 50 random patients who met our algorithm and 45 had physician-confirmed SARDs, resulting in a PPV of approximately 90%. Patients with osteoarthritis, fibromyalgia, or crystalline arthritis without another concomitant SARD diagnosis were excluded.

We included patients who received at least 2 doses of BNT162b2 or at least 2 doses of mRNA-1273. Those who received a Ad26.CoV2.S (Janssen/Johnson & Johnson) vaccine at any time or who received mixed doses (eg, an individual who received an initial dose of Ad26.CoV2.S and then a dose of mRNA-1273 or BNT162b2) of any vaccine type were excluded from analysis. We included patients with a COVID-19 infection prior to the index date. Patients were followed from index date until the date of positive SARS-CoV-2 test result (PCR or antigen), death, or end of follow-up (February 22, 2022).

*Outcomes.* The primary outcome was SARS-CoV-2 breakthrough infection, defined as follows: (1) a positive SARS-CoV-2 PCR or antigen test from a nasopharyngeal or respiratory specimen, and/or (2) a positive COVID-19 flag in the EHR on or after the index date. In MGB, a COVID-19 flag indicates a confirmed diagnosis of SARS-CoV-2 infection and captures patients with a confirmed positive test outside of our healthcare system. We also included patients flagged as having COVID-19 based on a positive home rapid antigen assay reported to providers or clinics. In some cases, results from tests performed outside of MGB were automatically pulled into the EDW because of a linkage across other healthcare systems that also use Epic software as an EHR.

*Covariates.* Data regarding dates and presence of ICD-9 or ICD-10 codes, medication prescriptions, demographics, and comorbidities were extracted from the MGB EDW, as previously described.<sup>10,13</sup>

The patient's primary rheumatic disease diagnosis was based on ICD-9/10 codes. In some cases, patients had codes associated with multiple rheumatic diseases. In scenarios where one disease is often secondary to or associated with a primary condition (eg, antiphospholipid syndrome in systemic lupus erythematosus [SLE]), the patient was considered to have the primary disease (eg, SLE). In cases where there was a discrepancy (eg, giant cell arteritis [GCA] and antineutrophil cytoplasmic antibody-associated vasculitis), the disease associated with the ICD-9/10 code used most frequently was considered the primary diagnosis. Cases in which ICD-9/10 codes that can coexist (eg, seronegative spondyloarthritis and GCA) or can exist as overlap disease (eg, SLE and RA) were categorized as multiple primary rheumatic diseases. Since many patients had ICD-9/10 codes for both GCA and polymyalgia rheumatica, we considered this as a single combined category.

Medication data documented or prescribed in the EHR, was extracted as structured data within 12 months of the index date. Medications were categorized as being a csDMARD, bDMARD, tsDMARD, or oral glucocorticoid (GC).

Baseline characteristics including demographics (including race/ethnicity as obtained from the EHR), comorbidities as defined by ICD-9/10 codes, smoking history, and BMI were extracted from the EDW and assessed in the 1 year prior to the index date. We excluded 107 patients with missing BMI and 1 patient with missing smoking status. The Charlson Comorbidity Index (CCI) was calculated using all available data from comorbidities as ascertained by ICD-9/10 in the 1 year prior to the index date.<sup>14</sup>

**Statistical analyses.** Baseline characteristics were compared between patients who received either BNT162b2 or mRNA-1273 and are reported as frequencies and percentages or means and SDs. We determined incidence rates and 95% CIs of COVID-19 infections per 1000 person-months.

To account for potential confounding introduced by variation in vaccine administration and availability and fluctuation of COVID-19 infection rates over time, we used time-stratified propensity score (PS) overlap weighting. Eligible individuals were allocated into biweekly time blocks according to their index dates. We restricted the study period from December 27, 2020, to May 15, 2021, because there were too few patients in time blocks before and after this period to perform the procedure. In each time block, we calculated a PS using logistic regression models and adopted an overlap weighting approach to balance baseline characteristics.<sup>15,16</sup> Potential confounders were selected based on prior literature and clinical expertise and included COVID-19 infection prior to index date, age, sex, race, ethnicity, BMI, smoking status, CCI, rheumatic disease, immunomodulatory medication categories (eg, bDMARD, tsDMARD, csDMARD, rituximab [RTX]), and GCs (Table 1). Given the known significant effects of B cell depletion on humoral immune responses to mRNA vaccine, we specifically included RTX exposure as a covariate.<sup>17,18</sup> Because of the size of the sample included, we were unable to incorporate other specific medications into the PS. For each person, we included all medication categories documented or prescribed in the 12 months preceding the index date in the PS to reflect the characteristic and severity of their disease. Patients receiving the BNT162b2 vaccine were weighted by the probability

of not receiving the BNT162b2 vaccine (ie, 1-PS) and those receiving the mRNA-1273 vaccine were weighted by the probability of receiving the BNT162b2 vaccine (ie, PS). Overlap weights were bounded and smoothed to reduce the influence of individuals at the tails of the PS distribution without making any exclusions. To compare the distribution of covariates before and after weighting, we report standardized mean differences (SMDs).

We calculated the rate difference and 95% CIs per 1000 person-months and estimated hazard ratios (HRs) and 95% CIs using overlap PS-weighted Cox proportional hazard models of the time from index date to breakthrough infection or date of censoring. We accounted for the competing risk of death using the Fine-Gray method and confirmed that the proportional hazards assumption was met using a Kaplan-Meier method with an inverse probability weighting method.

We performed 3 sensitivity analyses to assess the robustness of our findings. First, we censored follow-up on December 15, 2021, the date that Omicron became the dominant variant in Massachusetts. Second, we censored follow-up at the time of a third vaccine dose. Third, we censored follow-up at the time of the earliest of the third vaccine dose or December 15, 2021. We also performed 2 negative control analyses to assess for the effect of residual confounding. First, we assessed the risk of COVID-19 within 10 days of the first vaccination when there should be no difference in the risk of breakthrough infection if confounding has been adequately addressed. Second, we compared death not attributed to COVID-19 in each vaccine group since vaccine type should not influence non-COVID-19-related mortality. All *P* values were 2-sided and *P* < 0.05 was considered significant for all tests. All statistical analyses were performed with SAS software, version 9.4 (SAS Institute).

**Table 1.** Demographic and clinical characteristics of patients with SARDs who received either BNT162b2 or mRNA-1273 vaccine (N = 9838).

	Before PS Overlap Weighting			After PS Overlap Weighting <sup>a</sup>		
	BNT162b2, n = 5516	mRNA-1273, n = 4322	Standardized Difference	BNT162b2, n = 5516	mRNA-1273, n = 4322	Standardized Difference
COVID-19 prior to index date, %	4.5	3.8	0.03	4.0	4.0	< 0.001
Age, yrs, mean (SD)	61 (15)	61 (15)	0.004	61 (9)	61 (11)	< 0.001
Female sex, %	74.5	75.8	0.03	75.2	75.2	< 0.001
White race, %	81.9	85.2	0.09	84.5	84.5	< 0.001
Hispanic or Latinx ethnicity, %	7.1	5.6	0.04	5.7	5.7	< 0.001
BMI, kg/m <sup>2</sup> , mean (SD)	28 (7)	29 (7)	0.05	28.6 (4.2)	28.6 (4.7)	< 0.001
Ever smoker, %	43.4	42.7	0.01	43.6	43.6	< 0.001
CCI, mean (SD)	2.6 (3)	2.3 (2.7)	0.08	2.5 (1.8)	2.5 (2.0)	< 0.001
RD diagnosis, %						
Rheumatoid arthritis	52.4	54.8	0.05	54.1	54.1	< 0.001
Other inflammatory arthritis	16.9	17.8	0.02	17.0	17.0	< 0.001
Systemic lupus erythematosus	13.5	11.6	0.06	12.2	12.2	< 0.001
Vasculitis	6.0	5.7	0.02	5.9	5.9	< 0.001
Other RD	5.0	4.6	0.02	4.7	4.7	< 0.001
Multiple RDs	6.2	5.7	0.03	6.0	6.0	< 0.001
Immunomodulatory medication, %						
csDMARDs <sup>b</sup>	74.0	73.6	0.01	74.3	74.3	< 0.001
bDMARDs <sup>c</sup>	42.7	43.3	0.01	42.5	42.5	< 0.001
Rituximab	2.3	2.3	0.003	2.1	2.1	< 0.001
tsDMARDs <sup>d</sup>	6.7	5.7	0.04	5.8	5.8	< 0.001
Oral glucocorticoid	11.4	9.5	0.06	10.0	10.0	< 0.001

<sup>a</sup> All variables listed were included in the PS models. <sup>b</sup> csDMARDs: azathioprine, methotrexate, leflunomide, mycophenolic acid, mycophenolate mofetil, sulfasalazine, hydroxychloroquine, chloroquine. <sup>c</sup> bDMARDs: ocrelizumab, abatacept, infliximab, etanercept, adalimumab, certolizumab, golimumab, anakinra, canakinumab, mepolizumab, benralizumab, tocilizumab, sarilumab, secukinumab, ixekizumab, ustekinumab, guselkumab, belimumab, eculizumab. <sup>d</sup> tsDMARDs: tofacitinib, baricitinib, upadacitinib. bDMARD: biologic DMARD; CCI: Charlson Comorbidity Index; COVID-19: coronavirus disease 2019; csDMARD: conventional synthetic DMARD; DMARD: disease-modifying antirheumatic drug; PS: propensity score; RD: rheumatic disease; SARD: systemic autoimmune rheumatic disease; tsDMARD: targeted synthetic DMARD.

## RESULTS

Among the 2.1 million vaccinated patients within MGB, we identified 5516 patients who received BNT162b2 and 4322 patients who received mRNA-1273 during the study period among patients with SARDs on immunomodulatory medications (Figure 1). Prior to PS weighting (Table 1), the 2 groups were overall similar. The mean (SD) age was 61 (15) years in each group (SMD 0.03). There were slight differences in the distribution of sex (75% vs 76%, SMD 0.004), proportion of White race (82% vs 85%, SMD 0.09) and Hispanic ethnicity (7% vs 6%, SMD 0.04). There were also differences in disease-specific features, including the CCI (mean 2.6 vs 2.3, SMD 0.08), proportion with RA (52% vs 55%, SMD 0.05), and proportion using certain immunomodulators such as tsDMARDs (6% vs 7%, SMD 0.04) and GCs (11% vs 10%, SMD 0.06). A slightly higher proportion of BNT162b2 recipients had a COVID-19 infection prior to vaccination than mRNA-1273 recipients (4.4% vs 3.8%, SMD 0.03). After PS weighting, there were no longer significant differences in the distribution of demographic and disease-specific characteristics, including for DMARD categories, among those who received BNT162b2 vs mRNA-1273, all with SMD < 0.001 (Table 1).

In our primary analysis, inclusive of a time period characterized by dominance of the Omicron variant in Massachusetts, there were 446 breakthrough infections among BNT162b2 recipients and 329 among mRNA-1273 recipients over a mean of 11 and 12 months of follow-up, respectively (Table 2). The weighted incidence of breakthrough infection was 6.83 vs 6.12 per 1000 person-months in BNT162b2 vs mRNA-1273

recipients, respectively. There was no statistically significant difference in the rate of breakthrough infection with BNT162b2 vs mRNA-1273 vaccination (weighted rate difference 0.71, 95% CI -0.70 to 2.12 per 1000 person-months) or the hazard ratio (HR) when comparing vaccine recipients (weighted HR 1.12, 95% CI 0.90 to 1.39; Figure 2).

We performed several sensitivity analyses and 2 negative control analyses to assess the robustness of our observations (Table 2). When we limited follow-up to the pre-Omicron era, there was a nonstatistically significant trend toward higher risk of breakthrough infection associated with BNT162b2 vs mRNA-1273 (weighted HR 1.34, 95% CI 0.91 to 1.98). Similar estimates were observed when we censored at the time of a third mRNA vaccine dose and when we censored at either the time of a third mRNA vaccine or the date when Omicron became the dominant strain in Massachusetts. There was no difference in the risk of breakthrough infection within 10 days of the index date when comparing BNT162b2 vs mRNA-1273 vaccine recipients (weighted HR 0.67, 95% CI 0.09 to 5.28). There was also no difference in recipients of BNT162b2 vs mRNA-1273 in the risk of death from causes other than COVID-19 (weighted HR 1.01, 95% CI 0.62 to 1.64).

## DISCUSSION

Among patients with SARDs on immunomodulatory medications, there was no statistical difference in the risk of breakthrough infection after 2 doses of either BNT162b2 or mRNA-1273. There was a trend in the pre-Omicron era toward mRNA-1273 providing a greater protection against breakthrough infection, but this did not reach statistical significance. Although ongoing efforts are being made to further reduce the risk of breakthrough infection and severity among patients with SARDs, the choice of mRNA vaccine type does not appear to be a strong factor driving this risk. Patients with SARDs initiating the vaccine series should be encouraged to receive whichever mRNA vaccine is available.

Previous studies have established that certain immunomodulator users have a blunted humoral immune response to SARS-CoV-2 vaccines, including the BNT162b2 and mRNA-1273 vaccines, and that this can increase the risk of breakthrough infection.<sup>6</sup> A recent study found that among immunomodulator users, mRNA-1273 may yield a greater level of humoral immunity than BNT162b2.<sup>8</sup> In the population managed in the VA system in the United States, investigators found a small but statistically significant association between BNT162b2 vs mRNA-1273 with the risk of breakthrough infection (risk ratio 1.27, 95% CI 1.15-1.42) over 24 weeks.<sup>8</sup> This population was different than ours since it included patients who were, on average, 10 years older and the majority of whom were male. Given these differences and observations regarding the blunted immunogenicity of mRNA vaccines in immunomodulator users compared to the general population,<sup>3,4</sup> it has been unclear whether BNT162b2 or mRNA-1273 provides greater protection against breakthrough infection. Our study expands upon prior findings by estimating similar effectiveness of both currently available

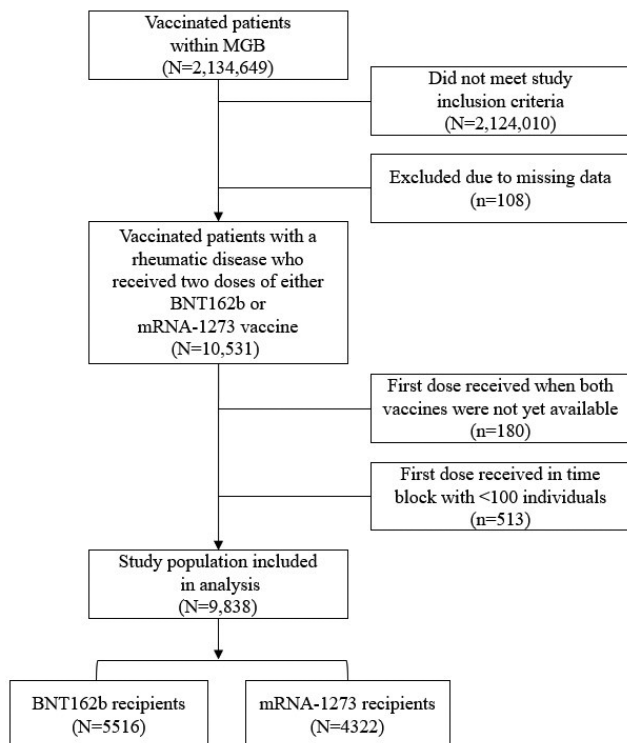


Figure 1. Identification of patients with a systemic autoimmune rheumatic disease who received either BNT162b2 or mRNA-1273 vaccines within the MGB system. MGB: Mass General Brigham.

Table 2. Risk of COVID-19 breakthrough infection among patients with SARDs who received either BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccine.

Population	No. of COVID-19 Breakthrough Infection Events		Mean Follow-up, months		IR <sup>a</sup> , per 1000 person-months		RD <sup>a</sup> (95% CI), per 1000 person-months	HR <sup>a</sup> (95%CI) BNT162b2 vs mRNA-1273
	BNT 162b2	mRNA-3 127	BNT 162b2	mRNA-1273	BNT 162b2	mRNA-1273		
	N	5516	4322	5516	4322	5516		
Primary analysis								
Any infection	446	329	11	12	6.83	6.12	0.71 ( -0.70 to 2.12)	1.12 (0.90 to 1.39)
Sensitivity analyses								
Pre-Omicron (12/15/2021)	158	94	9	10	2.89	2.16	0.73 ( -0.24 to 1.71)	1.34 (0.91 to 1.98)
Censor at 3rd vaccine	212	132	8	9	4.22	3.36	0.82 ( -0.43 to 2.07)	1.31 (0.94 to 1.83)
Pre-Omicron and censor at 3rd vaccine	118	71	8	8	2.49	1.95	0.55 ( -0.45 to 1.55)	1.32 (0.84 to 2.08)
Negative control analyses								
Infection within 10 days of first vaccine	6	5	12	12	0.06	0.09	-0.03 ( -0.18 to 0.12)	0.67 (0.09 to 5.28)
Death due to non-COVID-19 causes	97	60	11	12	1.28	1.27	0.01 ( -0.61 to 0.63)	1.01 (0.62 to 1.64)

<sup>a</sup>Time-stratified PS overlap weighted. PS model: COVID-19 prior to index date, age, sex, race, ethnicity, BMI, smoking status, Charlson Comorbidity Index, rheumatic disease diagnosis, immunomodulatory medication. COVID-19: coronavirus disease 2019; HR: hazard ratio; IR: incidence rate; PS: propensity score; RD: rate difference; SARD: systemic autoimmune rheumatic disease.

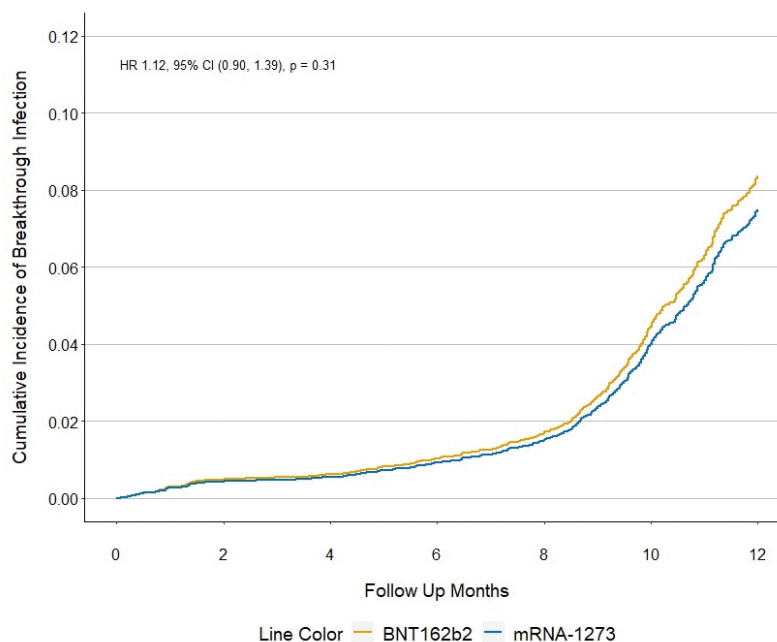


Figure 2. Cumulative incidence of COVID-19 breakthrough infections among patients with SARDs according to vaccine type (mRNA-1273 vs BNT162b2) through February 22, 2022. COVID-19: coronavirus disease 2019; HR: hazard ratio.

mRNA vaccines on the risk of breakthrough infection. However, our study may have been too small to detect modest statistically significant differences between the vaccine types.

A study by Widdifield et al examined COVID-19 vaccine effectiveness in patients with RA, ankylosing spondylitis, psoriasis, and inflammatory bowel disease and found that mRNA-1273 tended to have greater effectiveness than BNT162b2.<sup>3</sup> Several important aspects distinguish our study. First, all patients in our analysis were immunomodulator users

whereas these data were unavailable in the study by Widdifield et al,<sup>3</sup> so the balance of this important confounder between groups is unknown. Second, our study used robust methods to account for the differences in the temporal availability and uptake of these vaccines which could affect associations. Third, our study extended follow-up to include a time period characterized by Omicron variant dominance, which is now known to be associated with greater immune evasiveness.<sup>19</sup> Finally, theirs was focused on vaccine effectiveness (ie, vaccinated vs not vaccinated

for risk of infection), whereas ours assessed the risk of breakthrough infection between vaccine types.

In mid-December 2021, the Omicron variant became the dominant strain in Massachusetts and mRNA vaccines are now known to provide less protection against this variant because of spike protein mutations. Because of the known immune evasiveness associated with the Omicron variant,<sup>19</sup> we also examined outcomes limited to the pre-Omicron era and found that there was a trend toward mRNA-1273 having potentially greater efficacy during time periods characterized by dominance of Alpha and Delta variants. Collectively, these results do raise the question of whether the enhanced immunogenicity observed in patients with mRNA-1273 vs BNT162b2 provides greater protection for infection against variants more closely related to the original SARS-CoV-2 strain used to develop vaccines.<sup>9</sup> Our findings did not achieve statistical significance but should be evaluated again in the future in the context of the anticipated use of variant-specific vaccines.

Our study has a number of notable strengths. First, we systematically identified patients with SARDs who used immunomodulators prior to vaccination as well as test-confirmed COVID-19 breakthrough infection using data from tests conducted in the healthcare setting and at home. Second, we used time-stratified PS overlap weighting to account for potential confounding introduced by variation in vaccine availability and fluctuation of COVID-19 infection rates over time as well as potential differences in demographic, lifestyle, and clinical characteristics. Third, we assessed the robustness of our findings in 2 negative control analyses to investigate any potential strong impact of unmeasured confounding.

Despite these strengths, our study has certain limitations. First, we identified patients who had been prescribed an immunomodulator prior to receiving an mRNA vaccine; however, we did not have data on whether an individual was actually taking their prescription at the time of vaccination, the dose of steroid at the time of vaccination, or whether patients had temporarily held their treatments around the time of vaccination, as has been recommended.<sup>20</sup> Regardless, we would not expect the patterns of holding medications to differ among those who received either mRNA vaccine. Second, the number of patients in potential subgroups of interest (eg, specific immunomodulator use) was small, limiting our ability to compare mRNA vaccine effectiveness among users of immunomodulators associated with different degrees of blunted immune responses and to incorporate some of these specific variables into our propensity scores. Third, we did not have data regarding antibody or other immunologic responses to the vaccine. Fourth, we may not have detected all breakthrough infections, particularly those who tested positive on home rapid antigen tests but never reported to their MGB physician. Although this potential missing information may underestimate the absolute rate of breakthrough infections, it is unlikely that this varies by vaccine type and so should not affect our results. Fifth, we did not have data regarding disease activity; however, we would not expect this to vary by vaccine type. Further studies with registry data may be necessary to explore disease activity, vaccination, and breakthrough infections.

In conclusion, we found that the BNT162b2 and mRNA1274 vaccines have comparable effectiveness with regard to the risk of breakthrough infection among patients with SARDs using immunomodulators. There may be a benefit to mRNA1274 over BNT162b2, but this was substantially blunted in a time period characterized by Omicron dominance. The choice of mRNA vaccine type is unlikely to strongly influence the risk of breakthrough infection in this population and the decision regarding which mRNA vaccine to receive should be based on availability rather than potential difference in effectiveness.

## ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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