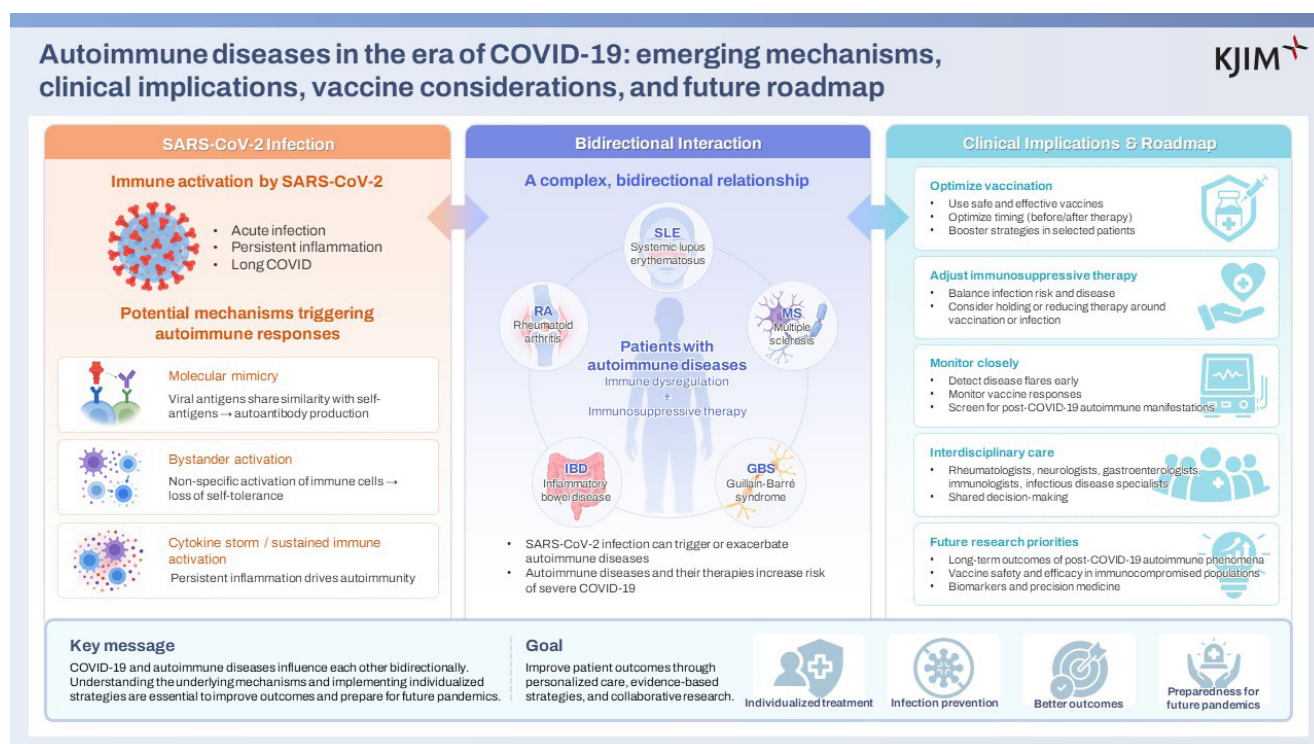


Autoimmune diseases in the era of COVID-19: emerging mechanisms, clinical implications, vaccine considerations, and future directions

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The coronavirus disease 2019 (COVID-19) pandemic has highlighted a complex, bidirectional relationship between SARS-CoV-2 infection and autoimmune diseases. This review examines how SARS-CoV-2 infection influences the incidence, progression, and outcomes of five major autoimmune conditions: systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, and Guillain-Barré syndrome. Patients with autoimmune diseases are at increased risk of severe COVID-19 due to intrinsic immune dysregulation and the use of immunosuppressive therapies, both of which impair antiviral host defenses. Conversely, COVID-19 has been implicated in the initiation and exacerbation of autoimmune responses through mechanisms such as molecular mimicry and bystander activation. Concerns have also arisen regarding the safety and efficacy of COVID-19 vaccines in immunocompromised populations. Although vaccines are generally tolerated in these individuals, certain immunosuppressive therapies may attenuate humoral and cellular immune responses. Strategies such as adjusting immunosuppressive regimens and optimizing the timing of vaccination have been proposed to improve vaccine efficacy. Disease-specific considerations are essential to balance infection risk with adequate control of autoimmune activity. Overall, this review underscores the importance of individualized treatment strategies, close clinical monitoring, and interdisciplinary care in managing patients with autoimmune diseases during the COVID-19 pandemic. A deeper understanding of these interactions will be critical for improving patient outcomes and preparing for future pandemics involving immune-mediated diseases.

Keywords: Autoimmune diseases; COVID-19; Immunosuppressive therapy; Vaccine; Immune system diseases

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has posed unprecedented challenges to global health systems [1,2]. Beyond its acute respiratory manifestations, COVID-19 has revealed complex immunological interactions with pre-existing conditions, including autoimmune diseases [3]. Autoimmune diseases, characterized by immune-mediated tissue damage and loss of self-tolerance [4], are increasingly recognized as important comorbidities in COVID-19 [5]. Notably, autoimmune diseases and COVID-19 share several key immunological features, including dysregulated cytokine production, lymphocyte dysfunction, and impaired regulatory immune control [6,7]. An immune phenotyping study suggests that long COVID is associated with persistent alterations in both innate and adaptive immune compartments, accompanied by broadly enhanced humoral responses [8]. In severe cases requiring intensive care, patients exhibit a profoundly altered immune profile characterized by sustained lymphopenia, expansion of granulocytes and plasmablasts, increased activation and terminal differentiation of T cells and natural killer cells, and markedly elevated SARS-CoV-2-specific antibody responses [9].

The relationship between COVID-19 and autoimmune diseases is increasingly recognized as bidirectional [10]. In-

dividuals with autoimmune diseases are at increased risk of SARS-CoV-2 infection and adverse clinical outcomes [11]. This vulnerability is attributable to their immunocompromised state and is further influenced by the use of immunosuppressive therapies. Corticosteroids, while essential for controlling autoimmune activity, may impair viral clearance and increase the risk of severe COVID-19 outcomes [12]. Conversely, SARS-CoV-2 infection has been implicated in the initiation and exacerbation of autoimmune conditions, potentially through mechanisms such as molecular mimicry and bystander activation [13-15]. Observational studies have also reported an increased risk of incident autoimmune diseases following SARS-CoV-2 vaccination [5,16]. Furthermore, concerns have been raised regarding the safety and immunogenicity of COVID-19 vaccines in patients with autoimmune diseases [17-19].

This narrative review aims to comprehensively examine the immunological relationship between COVID-19 and five major autoimmune diseases: systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), multiple sclerosis (MS), inflammatory bowel disease (IBD), and Guillain-Barré syndrome (GBS). It further evaluates how autoimmune pathophysiology and immunomodulatory treatments influence susceptibility to SARS-CoV-2, and how SARS-CoV-2 infection may contribute to the onset, reactivation, or exacerbation of autoimmune diseases.

BIDIRECTIONAL ASSOCIATION BETWEEN AUTOIMMUNE DISEASES AND COVID-19

Individuals with autoimmune diseases are at increased risk of severe COVID-19 outcomes due to intrinsic immune dysregulation and the use of immunosuppressive therapies [20]. Autoimmune diseases are characterized by a breakdown in self-tolerance, leading to chronic activation of autoreactive T and B lymphocytes, impaired regulatory T-cell function, and dysregulated cytokine signaling [4]. These alterations weaken antiviral defense mechanisms, resulting in an increased susceptibility to infections, including SARS-CoV-2. Upon the entry of SARS-CoV-2, the innate immune system is rapidly activated, with induction of type I interferons and subsequent release of proinflammatory cytokines such as interleukin (IL)-6, IL-1 β , and tumor necrosis factor (TNF)- α [21]. In some cases, however, this response becomes excessive, leading to a cytokine storm, a hyperinflammatory state resembling macrophage activation syndrome, although not necessarily representing a direct exacerbation of autoimmune disease activity [22]. Moreover, SARS-CoV-2 infection has been shown to induce lymphopenia, particularly affecting CD4⁺ and CD8⁺ T cells, further compromising immune regulation [23]. The combination of pre-existing immune dysregulation and viral infection—which may disrupt interferon signaling, impair effective T-cell-mediated responses, and delay viral clearance—can increase vulnerability to severe COVID-19 outcomes in individuals with autoimmune diseases [12]. Many of these patients are treated with immunosuppressive agents, including corticosteroids and disease-modifying antirheumatic drugs (DMARDs) [24]. Although essential for disease control, these therapies can further impair host immunity, weakening antiviral defenses. This risk appears particularly elevated in patients receiving high-dose corticosteroids or B cell-depleting agents, such as rituximab [25,26].

Growing evidence suggests that COVID-19 itself may trigger or exacerbate autoimmune diseases [27]. During severe SARS-CoV-2 infection, many individuals develop autoantibodies, including antinuclear antibodies, antiphospholipid antibodies, and anti-type I interferon antibodies [28-30]. Mechanisms such as molecular mimicry, bystander activation, and epitope spreading may underlie these responses, suggesting that SARS-CoV-2 can induce or amplify autoimmunity [31,32]. Notably, 28 human proteins with regions homologous to SARS-CoV-2 peptides have been identified,

which may act as potential autoantigens in individuals who develop autoimmune conditions following infection [33]. Through these mechanisms, COVID-19 may initiate or exacerbate pre-existing autoimmune diseases. Consistently, large population-based studies have shown that individuals with COVID-19 have a significantly higher risk of developing a range of autoimmune diseases compared with uninfected individuals [5,27,34].

SARS-CoV-2 vaccination is a key strategy for protecting immunocompromised individuals; however, its effectiveness in patients with autoimmune diseases requires careful consideration [35,36]. Patients receiving immunosuppressive therapies often exhibit reduced antibody responses to COVID-19 vaccines [37]. For example, individuals treated with rituximab or methotrexate may fail to mount adequate neutralizing antibody responses following mRNA vaccination [38,39]. Methotrexate, in particular, has been shown to impair both humoral and cellular immune responses to mRNA-based COVID-19 vaccines [40,41]. Similarly, in previously vaccinated individuals, initiation of rituximab therapy is associated with a progressive decline in anti-SARS-CoV-2 spike antibody titers [42,43]. Janus kinase (JAK) inhibitors may also attenuate vaccine-induced T-cell responses [44]. This reduced immunogenicity is clinically relevant, as it may increase the risk of breakthrough infections and post-acute sequelae of SARS-CoV-2 infection (long COVID) [45]. Clinical outcomes also vary according to the immunosuppressive regimen used; rituximab and JAK inhibitors have been more strongly associated with poor COVID-19 outcomes than other biologic or targeted synthetic DMARDs [46]. Strategies to improve vaccine responses include temporary modification of immunosuppressive therapy; for example, a two-week discontinuation of methotrexate after booster vaccination has been shown to enhance antibody production [47]. Other approaches include optimizing vaccination timing, such as completing primary vaccination before initiating B cell-depleting therapy [48], briefly pausing methotrexate after vaccination [47], and administering booster doses when indicated [49]. Figure 1 illustrates the bidirectional interactions between SARS-CoV-2 infection and autoimmune diseases.

SLE

SLE is a chronic autoimmune disease characterized by inflam-

mation and immune-mediated damage affecting multiple organ systems, including the mucocutaneous, musculoskeletal, hematologic, and renal systems [50]. Approximately 3.4 million individuals worldwide are affected by SLE [51]. SLE has long been associated with viral triggers, and COVID-19 has likewise been shown to influence its clinical course in several ways [5,52,53]. Chang et al. [5] reported that individuals with COVID-19 had a significantly increased risk of developing new-onset SLE (hazard ratio [HR], 2.98). Similarly, a population-based study conducted in Paris, France, found that patients with COVID-19 had a higher risk of SLE flares compared with uninfected individuals (HR, 3.79) [52].

Patients with SLE are also at increased risk of SARS-CoV-2 infection and severe COVID-19 outcomes. Data from the Global Rheumatology Alliance registry identified age, sex, comorbidities, disease activity, and treatment status as key determinants of COVID-19 severity in patients with SLE, with steroid use and treatment interruption particularly associated with worse outcomes [53]. Another study reported that individuals with SLE have higher risks of SARS-CoV-2 infection (0.6–22%), COVID-19-related hospitalization (30%), and mortality (6.5%) compared with individuals without SLE [54].

Despite these associations, a Mendelian randomization

study by Yang et al. found no evidence of a direct genetic causal relationship between COVID-19 and SLE [55]. Nevertheless, shared biological mechanisms, such as similar macrophage activation pathways and features of gut microbial dysregulation, have been proposed for both conditions [55]. Regarding vaccination, SARS-CoV-2 vaccines are generally safe in patients with SLE and elicit adequate immune responses, even in the context of immunosuppressive therapy [56–59]. However, certain agents, including mycophenolate, tacrolimus, and belimumab, may reduce antibody responses [58]. Notably, temporary discontinuation of mycophenolate for one week has been associated with improved vaccine immunogenicity (Table 1) [58].

RA

RA is a systemic autoimmune disorder primarily affecting the joints and periarticular soft tissues, characterized by persistent synovial inflammation and progressive joint destruction [60]. Emerging evidence suggests that SARS-CoV-2 infection may trigger the onset of RA [5,61,62]. A case series described five patients who developed inflammatory arthritis resembling RA within weeks of acute SARS-CoV-2 infection [61]. Pop-

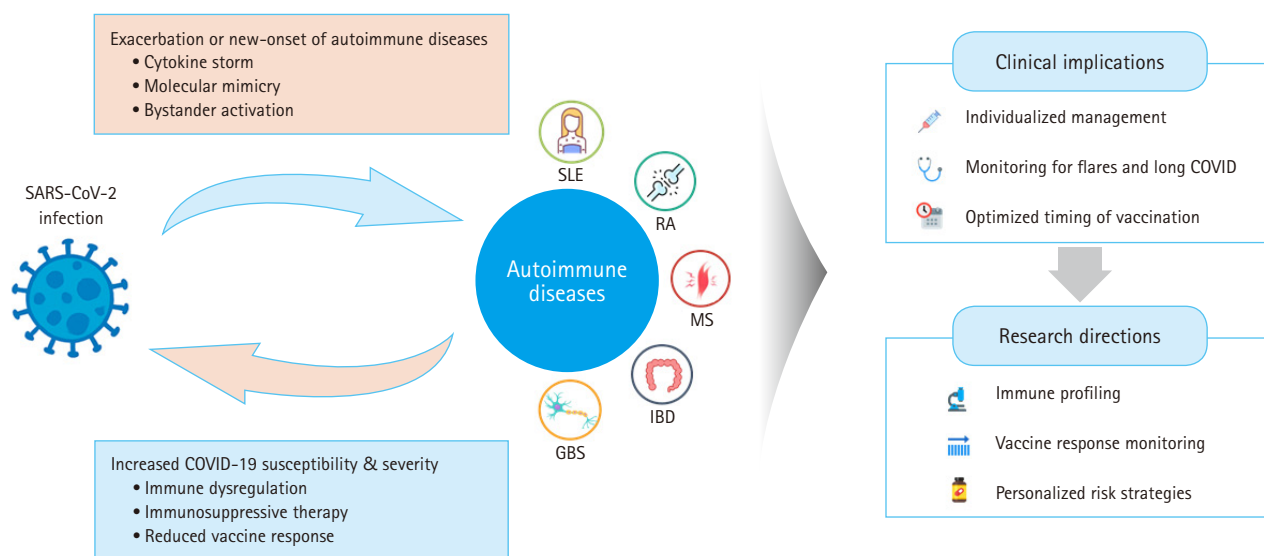


Figure 1. Bidirectional interactions between SARS-CoV-2 infection and autoimmune diseases. SARS-CoV-2 infection may trigger the onset or exacerbate the course of autoimmune diseases through multiple immunopathogenic mechanisms, including molecular mimicry, cytokine storm, bystander activation, and autoantibody production. Conversely, individuals with pre-existing autoimmune diseases, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), multiple sclerosis (MS), inflammatory bowel disease (IBD), and Guillain-Barré syndrome (GBS), are at increased risk of severe COVID-19 outcomes due to underlying immune dysregulation and the use of immunosuppressive therapies. These bidirectional interactions underscore the importance of individualized vaccination strategies, tailored immunomodulatory treatment, and close clinical monitoring in this vulnerable population.

ulation-based studies have also reported an increase in RA incidence following SARS-CoV-2 infection [62]. Chang et al. [5] further demonstrated that individuals infected with SARS-CoV-2 had a significantly increased risk of developing RA (HR, 2.98).

Conversely, individuals with pre-existing RA are at increased risk of adverse COVID-19 outcomes. A USA cohort study reported higher risks of hospitalization (relative risk [RR], 1.14) and intensive care unit (ICU) admission (RR, 1.32) among individuals with RA infected with SARS-CoV-2 compared with those without RA [63]. Similar findings have been reported in population-based studies from the UK [64,65], the USA [66], and Denmark [67]. This increased vulnerability persists even after vaccination, with vaccinated individuals with RA remaining at higher risk of SARS-CoV-2 infection and COVID-19-related hospitalization than vaccinated individuals without RA [65,67]. However, absolute risks are lower among vaccinated patients with RA than among those who are unvaccinated [67]. Observational studies suggest that COVID-19 vaccination is generally safe in patients with RA and is not associated with a clinically meaningful increase in disease activity [68,69].

The severity of COVID-19 in individuals with RA appears to vary according to the immunomodulatory treatment regimen. Notably, treatment with rituximab has been associated with worse outcomes independent of vaccination status, although these findings are based on a limited number of events [67]. Data from the COVID-19 Global Rheumatology Alliance registry further indicate that the use of rituximab and JAK inhibitors is associated with greater COVID-19 severity compared with the use of TNF inhibitors [46]. Glucocorticoids remain a cornerstone of RA management [60]; however, doses exceeding 10 mg/day of prednisone have been associated with an increased risk of severe COVID-19-related mortality (odds ratio [OR], 1.89) [70]. Taken together, these findings highlight the importance of personalized risk mitigation strategies in patients with RA, particularly those receiving high-risk immunosuppressive regimens.

According to meta-regression analyses by the Institute for Health Metrics and Evaluation (IHME), the global age-standardized incidence rate of RA in 2023 was estimated at 11.65 (95% uncertainty interval [UI], 10.56–13.02) per 100,000 population [71–73]. As the comprehensive Global Burden of Disease (GBD) 2023 dataset is not yet fully available, additional details on incidence rates and trends based on the GBD 2021 dataset are presented in Table 2 and

Figures 2 and 3. Overall, regions appear to have maintained their pre-pandemic incidence patterns following the onset of COVID-19 (Fig. 3) [71]. However, limitations in primary data collection during the pandemic, including delayed surveys and reporting disruptions, may introduce additional uncertainty into recent estimates, despite the use of model-based approaches designed to account for incomplete data [74]. These estimates reflect population-level disease burden and should be interpreted separately from individual-level risk estimates derived from observational studies (Table 1).

MS

MS is an autoimmune disease of the central nervous system with an incompletely understood etiology [75]. Both genetic and environmental factors have been implicated; notably, a recent study of USA military personnel reported a 32-fold increase in the risk of developing MS following Epstein–Barr virus (EBV) infection, but not after infection with other viruses, suggesting a potential causal role for EBV [76]. Evidence linking SARS-CoV-2 infection to the onset of MS remains limited. However, studies evaluating its impact on disease activity and progression in patients with MS have yielded heterogeneous findings [77–80]. A multicenter study conducted in Austria found no significant increase in relapse risk or disability progression following SARS-CoV-2 infection in patients with MS [77]. Similarly, Montini et al. reported no significant effects of COVID-19 on new MRI lesions, expanded disability status scale (EDSS) progression, relapse rate, or cognitive performance [78]. In contrast, a nationwide study from Iran found that although relapse rates remained unchanged in patients with relapsing-remitting MS (RRMS), both MRI lesion burden and EDSS scores increased significantly after infection [79]. Furthermore, an analysis from the National MS Center in Belgium suggested that COVID-19 may accelerate disability progression in patients with MS, particularly in cases of severe infection [80]. These discrepant findings likely reflect substantial heterogeneity in study design, patient populations, outcome definitions, disease severity, and follow-up duration. Taken together, current observational evidence on the impact of SARS-CoV-2 infection on MS disease activity and progression remains inconclusive. Meanwhile, the risk of SARS-CoV-2 infection in patients with MS appears to be comparable to that in the

Table 1. Comparative summary of the impact of COVID-19 across five major autoimmune diseases

Feature	SLE	RA	MS	IBD	GBS
Risk of flare/new onset after COVID-19	Increased risk of flare and new onset [5,52]	Increased incidence [5,61,62,121]	Conflicting results observed [77-80,85]	Insufficient evidence for causal association [93-96]	Increased incidence [108-111]
Risk of COVID-19 infection	Increased [54]	Increased [64,65]	Comparable to general population [81]	Comparable to general population [97,98]	N/A
Risk of COVID-19 severity	Increased severity and mortality [53,54]	Increased [63-67]	Increased severity and mortality [82,83,85]	Comparable to general population [97,98]	N/A
Vaccine safety	Generally safe [56-59]	Generally safe [68,69]	Generally safe [81]	Generally safe [98,100]	Increased GBS risk with Ad26.COV2. S and ChAdOx1-S; no association with mRNA vaccines [113-117]
Vaccine immunogenicity	Reduced antibody response with mycophenolate mofetil [58]	Reduced but substantial vaccine protection [67]	Reduced with anti-CD20 agents or S1P receptor modulators [81,88]	Generally preserved [101]	N/A
Impact of immunomodulatory therapies on COVID-19	N/A	Increased severity with rituximab, JAK inhibitors, and high-dose glucocorticoids [46,67,70]	Increased risk with anti-CD20 therapies [81-84,86], decreased risk with interferon therapy [87]	Increased hospitalization and mortality with 5-ASA and corticosteroids [97]	N/A

SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; MS, multiple sclerosis; IBD, inflammatory bowel disease; GBS, Guillain-Barré syndrome; S1P, sphingosine-1-phosphate; JAK, Janus kinase; 5-ASA, 5-aminosalicylic acid.

Table 2. Age-standardized incidence rates (per 100,000 population) for rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease from 2019 to 2021, presented globally and by region

Regions	Age-standardized incidence rate (95% UI)								
	Rheumatoid arthritis			Multiple sclerosis			Inflammatory bowel disease		
	2019	2020	2021	2019	2020	2021	2019	2020	2021
Global	11.75 (10.62–13.05)	11.78 (10.63–13.10)	11.80 (10.64–13.12)	0.78 (0.69–0.87)	0.78 (0.69–0.87)	0.78 (0.69–0.87)	4.45 (3.88–5.19)	4.45 (3.87–5.21)	4.45 (3.87–5.19)
Central Europe, Eastern Europe, and Central Asia	9.14 (8.13–10.20)	9.17 (8.15–10.25)	9.18 (8.18–10.26)	1.28 (1.18–1.40)	1.27 (1.17–1.40)	1.27 (1.17–1.40)	4.97 (4.27–5.92)	4.97 (4.31–5.90)	4.97 (4.29–5.93)
High-income	17.43 (15.94–19.09)	17.48 (15.98–19.16)	17.55 (16.07–19.18)	2.72 (2.49–2.97)	2.73 (2.49–2.98)	2.74 (2.49–2.99)	12.50 (10.94–14.54)	12.53 (10.93–14.58)	12.59 (10.99–14.59)
Latin America and Caribbean	14.30 (12.84–15.82)	14.18 (12.76–15.66)	14.26 (12.79–15.74)	0.65 (0.55–0.75)	0.65 (0.55–0.75)	0.65 (0.56–0.75)	1.79 (1.55–2.18)	1.80 (1.56–2.19)	1.81 (1.56–2.20)
North Africa and Middle East	5.44 (4.77–6.11)	5.48 (4.83–6.16)	5.52 (4.84–6.21)	1.58 (1.37–1.80)	1.57 (1.37–1.80)	1.59 (1.38–1.83)	3.14 (2.70–3.82)	3.16 (2.72–3.85)	3.18 (2.73–3.87)
South Asia	13.39 (11.83–15.19)	13.62 (12.03–15.45)	13.77 (12.15–15.66)	0.42 (0.35–0.49)	0.42 (0.35–0.50)	0.42 (0.35–0.50)	5.96 (5.18–7.15)	6.02 (5.23–7.18)	6.00 (5.21–7.23)
Southeast Asia, East Asia, and Oceania	10.81 (9.56–12.24)	10.82 (9.61–12.26)	10.82 (9.60–12.29)	0.17 (0.14–0.20)	0.17 (0.14–0.21)	0.17 (0.14–0.21)	1.17 (1.01–1.41)	1.18 (1.01–1.40)	1.18 (1.01–1.41)
Sub-Saharan Africa	5.35 (4.79–6.00)	5.39 (4.81–6.04)	5.42 (4.84–6.07)	0.34 (0.29–0.41)	0.35 (0.29–0.41)	0.35 (0.29–0.41)	1.61 (1.40–1.90)	1.61 (1.40–1.92)	1.62 (1.41–1.93)

UI, uncertainty interval.

Estimates are derived from the Global Burden of Disease Study 2021.

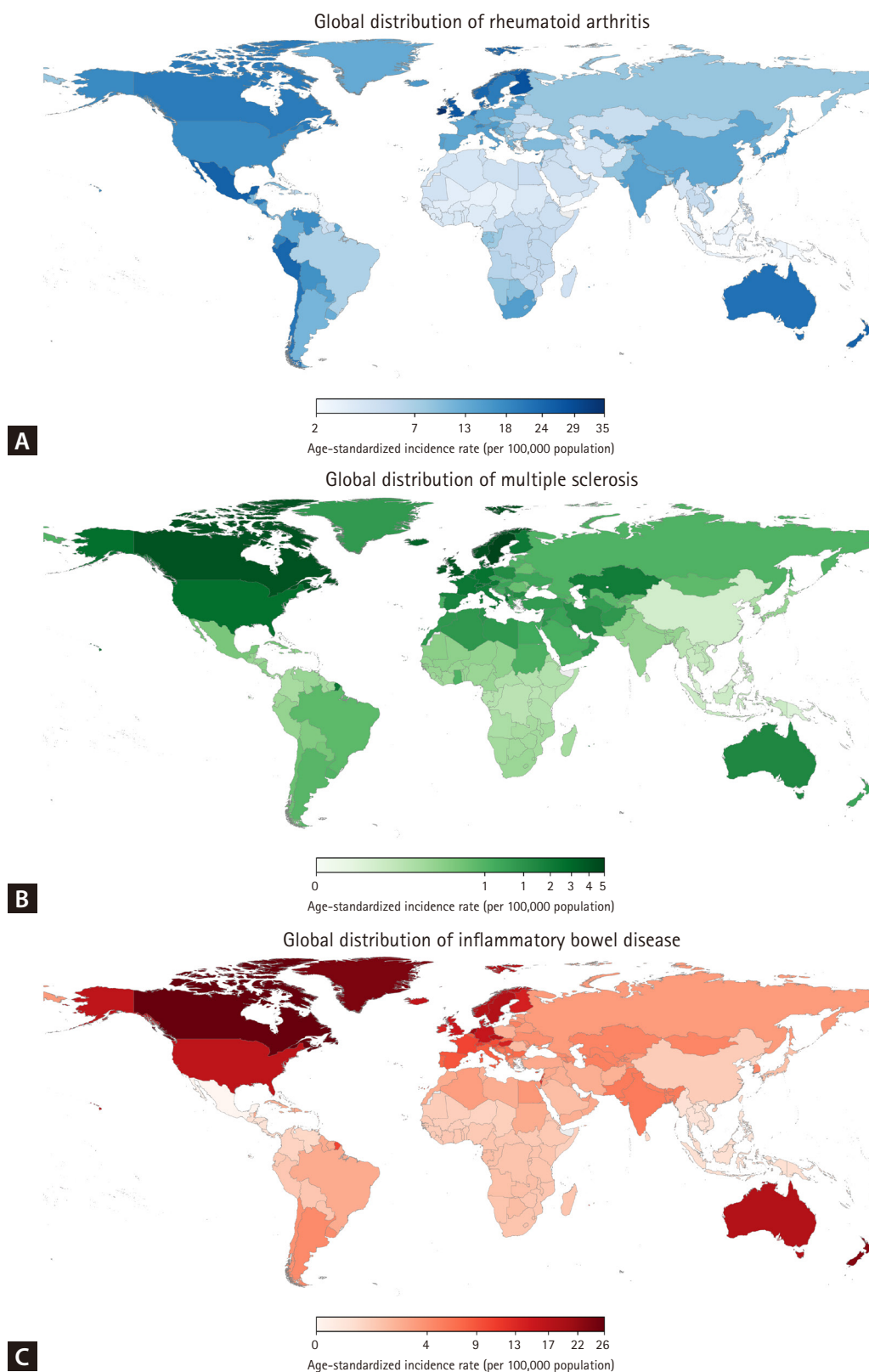


Figure 2. Global distribution of age-standardized incidence rates of (A) rheumatoid arthritis, (B) multiple sclerosis, and (C) inflammatory bowel disease in 2021. Estimates are derived from the Global Burden of Disease Study 2021.

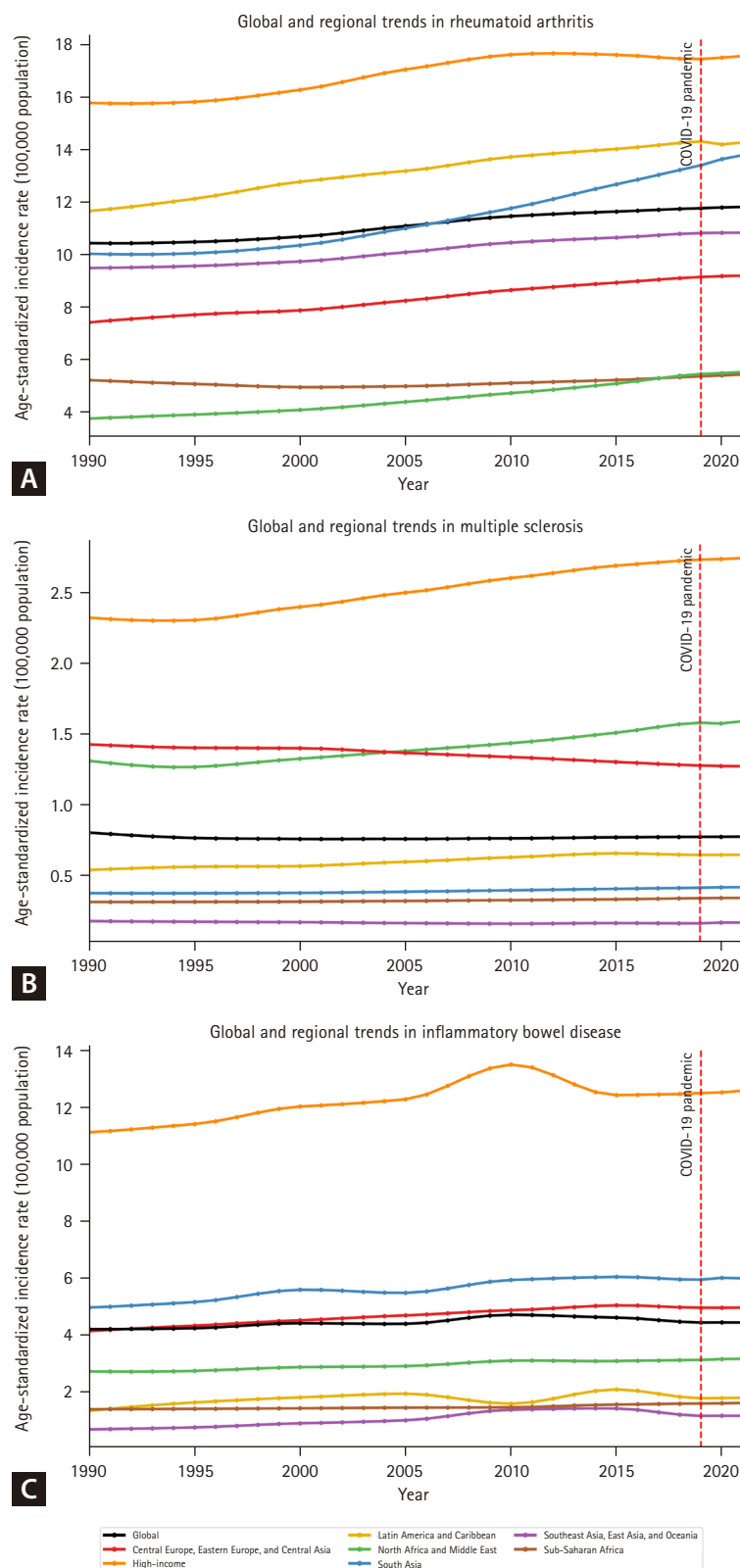


Figure 3. Global and regional trends in age-standardized incidence rates of (A) rheumatoid arthritis, (B) multiple sclerosis, and (C) inflammatory bowel disease from 1990 to 2021. The red dashed line indicates the onset of the COVID-19 pandemic. Estimates are derived from the Global Burden of Disease Study 2021.

general population [81].

Regarding clinical outcomes, an Italian cohort study reported that patients with MS had more than twice the risk of hospitalization, ICU admission, and death from COVID-19 compared with the general population [82]. This increased risk was more pronounced in high-risk subgroups [83]. In addition, patients with progressive MS appear to be at higher risk of severe COVID-19 than those with RRMS [83,84]. Mendelian randomization analysis by Baranova et al. further suggested a bidirectional causal relationship, whereby genetic liability to MS increased the risk of COVID-19 hospitalization, and genetic liability to severe COVID-19 increased the risk of MS [85]. Treatment-related factors also influence outcomes. Several studies have consistently shown that anti-CD20 therapies are significantly associated with an increased risk of severe COVID-19 [81-84,86]. This association was confirmed in a large pooled analysis of Italian and French cohorts, which also reported that interferon therapy was associated with a reduced risk of severe COVID-19 [87].

Regarding vaccination, COVID-19 vaccines are generally safe in patients with MS, with no evidence of increased relapse risk and high seroconversion rates [81]. However, reduced immunogenicity has been observed in patients receiving anti-CD20 therapies or sphingosine 1-phosphate receptor modulators [81,88].

According to estimates from the IHME, the global age-standardized incidence rate of MS in 2023 was 0.76 (95% UI, 0.68–0.83) per 100,000 population [72,73,89]. Detailed incidence data and trends based on the GBD 2021 dataset are presented in Table 2 and Figures 2 and 3. High-income countries, which showed increasing incidence rates prior to the pandemic, have continued this upward trend, whereas minimal variation has been observed in other regions (Fig. 3) [89]. These patterns should be interpreted with caution, since data gaps and reporting delays during the pandemic may have influenced recent estimates, despite the use of modeling approaches designed to account for incomplete data [74].

IBD

IBD comprises a group of chronic inflammatory disorders of the gastrointestinal tract with a growing global burden, primarily including ulcerative colitis (UC) and Crohn's disease (CD) [90]. UC is characterized by continuous mucosal

inflammation beginning in the rectum and extending proximally to varying extents. CD is a complex, chronic inflammatory condition that can affect any part of the gastrointestinal tract and varies in age of onset, anatomical distribution, and disease severity [91]. A nationwide population-based study from South Korea reported that individuals infected with SARS-CoV-2 had a higher risk of developing CD than uninfected individuals (HR, 1.68) [92]. Several cases of newly diagnosed UC and CD following SARS-CoV-2 infection have also been described; however, current evidence remains insufficient to establish a causal relationship between COVID-19 and the development of IBD [93-96].

Evidence does not indicate a substantially increased risk of SARS-CoV-2 infection among patients with IBD compared with the general population, and most studies report no significant differences in hospitalization rates, disease severity, or mortality [97,98]. In a subgroup analysis, Lee et al. [97] found that patients with CD had a lower risk of COVID-19-related hospitalization and death than those with UC. Most IBD therapies have not been associated with an increased risk of SARS-CoV-2 infection. However, the use of 5-aminosalicylates and systemic corticosteroids has been linked to higher risks of COVID-19-related hospitalization and mortality [97]. Additionally, a cohort study from Sicily identified severe IBD activity as a strong predictor of adverse COVID-19 outcomes in infected patients [99].

Regarding vaccination, current evidence indicates that neither mRNA nor vectored DNA vaccines worsen IBD [98,100]. Adequate seroconversion has also been observed in patients receiving anti-TNF therapy [101]. A multicenter, survey-based observational study conducted in Taiwan reported that patients with IBD expressed concerns about SARS-CoV-2 infection, disease severity, and potential vaccine-related adverse effects [102]. Some patients believed that immunomodulators, anti-TNF agents, or corticosteroids might increase infection risk and reported self-discontinuation of these therapies [102]. Notably, the study found that targeted educational interventions significantly alleviated these concerns [102]. Current evidence does not support a strong association between IBD and increased susceptibility to SARS-CoV-2 infection or greater COVID-19 severity, nor does it indicate that commonly used IBD therapies significantly increase infection risk [97,98,100,103]. Accordingly, proactive communication and patient education by health-care providers remain essential to address concerns regarding vaccination and treatment adherence in patients with

IBD.

According to estimates from IHME, the global age-standardized incidence rate of IBD in 2023 was 4.39 (95% UI, 3.80–5.13) per 100,000 population [72,73,90]. Detailed incidence data and trends based on the GBD 2021 dataset are presented in Table 2 and Figures 2 and 3. Overall, incidence rates remained stable across regions during the COVID-19 pandemic (Fig. 3) [90]. However, once again, these estimates should be interpreted with caution, since pandemic-associated disruptions in surveillance and data collection may have introduced additional uncertainty, despite the use of modeling approaches designed to account for incomplete data [74].

GBS

GBS is the most common acute paralytic neuropathy and is characterized as an autoimmune disorder in which the immune system targets peripheral nerves and spinal nerve roots [104,105]. Although its exact etiology remains unclear, most cases occur following viral or bacterial infections. Infection with *Campylobacter jejuni* is one of the most well-established risk factors, and viral infections, including Zika virus, have also been implicated [106]. Given its established association with viral infections, concerns have arisen regarding a potential link between SARS-CoV-2 infection and the development of GBS [107]. A study analyzing data from hospitals in northeastern Italy reported a 59% increase in GBS cases between March 2020 and March 2021 compared with the previous 13 months, with approximately half of these patients having a history of SARS-CoV-2 infection [108]. Similarly, an analysis of the U.S. Department of Veterans Affairs national healthcare database identified an increased risk of GBS within 12 months following acute SARS-CoV-2 infection (HR, 2.16) [109]. In Israel, SARS-CoV-2 infection was also associated with an elevated risk of GBS (OR, 6.30) [110]. These findings suggest that GBS may be triggered by immune-mediated mechanisms involving inflammatory cytokines such as TNF- α , IL-17, and IL-22, whose levels are elevated during SARS-CoV-2 infection [111].

The association between COVID-19 vaccination and GBS appears to vary by vaccine type [112–114]. Analysis of data from the U.S. Vaccine Adverse Event Reporting System indicated that the observed-to-expected ratio for GBS following Ad26.COV2.S vaccination was 3.79 at 21 days and 2.34 at

42 days post-vaccination, whereas no significant association was observed with mRNA vaccines (BNT162b2 and mRNA-1273) [112]. A study using the French National Health Data System similarly reported an increased risk of GBS following the first dose of ChAdOx1-S and Ad26.COV2.S vaccines, while no significant increase was observed with mRNA vaccines at the population level [113]. Similar results have been reported in analyses of the World Health Organization's global pharmacovigilance database [114] and in several systematic reviews [115,116]. Notably, a cohort study from Israel suggested that vaccination with BNT162b2 may be associated with a reduced risk of GBS [110]. Some studies have also reported a higher incidence of facial paralysis-associated GBS following vaccination, suggesting a possible link between specific vaccine platforms and GBS development [114,115].

COMPARISON AND CLINICAL IMPLICATIONS

The five autoimmune diseases discussed in this review (SLE, RA, MS, IBD, and GBS) share key immunopathological features but differ in their clinical course and vulnerability to COVID-19. A unifying characteristic across these conditions is immune dysregulation, often involving aberrant activation of autoreactive lymphocytes, heightened cytokine signaling, and breakdown of immune tolerance [4]. Shared inflammatory pathways include enhanced interferon signaling and IL-6-mediated systemic inflammation, which are prominently implicated in RA, MS, and IBD [117]. These mechanisms contribute to both increased susceptibility to infection and a propensity for exaggerated immune responses, particularly in the context of SARS-CoV-2. All five conditions are commonly managed with immunosuppressive therapies, ranging from corticosteroids and methotrexate to B cell-depleting agents and JAK inhibitors, each with distinct implications for COVID-19 severity and vaccine responsiveness [24].

Despite these shared features, important distinctions exist, although these should not be interpreted as rigid categories. SLE and RA are typically characterized by systemic immune activation and often require long-term immunosuppression [50,60], whereas MS and IBD are more organ-specific but increasingly treated with potent biologics that may impair antiviral immunity [75,90]. In contrast, GBS is generally post-infectious, representing a prototypical model of virus-triggered autoimmunity [106]. Treatment patterns

also differ across these conditions. Patients with RA and SLE frequently receive long-term corticosteroids and DMARDs, whereas those with MS and IBD more commonly rely on immune-modifying biologics [24]. These distinctions influence the degree and nature of infection risk, the likelihood that SARS-CoV-2 infection may act as a disease trigger, and the extent of vaccine responsiveness.

Effective patient management strategies should be disease-specific while guided by shared principles. Immunosuppressive therapy required continuous re-evaluation to balance disease control with infection risk and should be adapted when vaccine responses are likely to be impaired. Monitoring vaccine responses, considering booster doses, and ensuring interdisciplinary care coordination are essential components of comprehensive management. Healthcare systems should also implement tailored strategies to protect individuals with autoimmune diseases, including prioritization of booster vaccination programs [37,118], improved access to rapid diagnostic testing, and timely administration of antiviral therapies. Integration of rheumatology, neurology, and infectious disease services is critical for addressing key clinical challenges, such as adjusting immunosuppressive therapy during acute SARS-CoV-2 infection, distinguishing between disease flares and infection-related immune manifestations, and optimizing vaccination strategies in the context of ongoing immunomodulatory treatment. In parallel, strengthening electronic health record systems with a focus on interoperability across healthcare settings is essential to ensure that key clinical information, including immunosuppressive treatment history, vaccination status, and prior SARS-CoV-2 infection, is readily accessible regardless of where care is delivered. Improved data accessibility can facilitate real-time risk stratification and support coordinated, evidence-based clinical decision-making. Aligning clinical care with emerging evidence will be crucial to improving outcomes for individuals with autoimmune diseases, both in the context of long COVID and in preparation for future infectious disease threats. A comparative summary of the impact of COVID-19 on SLE, RA, MS, IBD, and GBS is presented in Table 1.

FUTURE RESEARCH DIRECTIONS OF AUTOIMMUNE DISEASES IN LONG COVID

The COVID-19 pandemic has led to the emergence of long

COVID, or post-acute sequelae of SARS-CoV-2 infection, characterized by persistent or new-onset symptoms lasting beyond 12 weeks after the initial infection [119]. Among its diverse clinical manifestations, autoimmune diseases have emerged as a significant concern [120]. Evidence from large-scale cohort studies indicates a strong association between SARS-CoV-2 infection and the subsequent development of autoimmune diseases [5,27,120]. Table 3 summarizes cohort studies evaluating these associations across multiple autoimmune conditions.

A German cohort study reported an increased incidence of new-onset autoimmune diseases within 3 to 15 months following SARS-CoV-2 infection (incidence rate ratio, 1.43) [121]. Similarly, a binational cohort study conducted in Korea and Japan identified elevated risks of autoimmune inflammatory rheumatic diseases (AIRD) after SARS-CoV-2 infection (HR, 1.25 in Korea and 1.79 in Japan) [120]. Another nationwide cohort study in Korea further highlighted the long-term risk of autoimmune and autoinflammatory connective tissue disorders following infection [13]. Using UK primary care data, a separate cohort study reported a 22% increase in the incidence of immune-mediated inflammatory diseases among individuals with COVID-19 compared with that in the general population [27].

COVID-19 severity has been associated with an increased risk of AIRD. Individuals with mild SARS-CoV-2 infection show an elevated risk (HR, 1.22), which increases further among those with moderate to severe infection (HR, 1.42) compared with that of uninfected individuals [120]. COVID-19 vaccination appears to confer a protective effect, significantly reducing AIRD risk among vaccinated individuals (HR, 0.59 after one dose; 0.42 after two or more doses) [120]. Similarly, a study conducted in Hong Kong reported reduced risks of several autoimmune diseases among vaccinated individuals [16]. Furthermore, higher risks were observed during periods dominated by more pathogenic variants, particularly the Delta variant [16].

Despite these advances, several important gaps and limitations remain. Short follow-up periods, typically less than one year, limit understanding of the long-term autoimmune consequences of SARS-CoV-2 infection. Additionally, most studies rely on single-country cohorts, restricting generalizability and limiting global comparisons across diverse populations. This limitation overlooks important differences in healthcare infrastructure, genetic susceptibility, and environmental exposures. Furthermore, variant-specific autoimmune

Table 3. Summary of cohort studies examining the association between SARS-CoV-2 infection and multiple autoimmune diseases

Country	Type of autoimmune disease	Autoimmune disease in the COVID-19 cohort		Autoimmune disease in the control cohort	Follow-up period	Risk of COVID-19 cohort compared to the control cohort
		Number of events ^{a)}	Number of events ^{a)}			
US [5]	Total	887,455	887,455		6 months	
	Rheumatoid arthritis	2,878	1,044			2.98 (2.78–3.20)
	Ankylosing spondylitis	243	82			3.21 (2.50–4.13)
	Systemic lupus erythematosus	1,189	429			2.99 (2.68–3.34)
	Dermatopolymyositis	131	72			1.96 (1.47–2.61)
	Systemic sclerosis	222	93			2.58 (2.02–3.28)
	Sjögren's syndrome	727	301			2.62 (2.29–3.00)
	Mixed connective tissue disease	139	48			3.14 (2.26–4.36)
	Behçet's disease	45	21			2.32 (1.38–3.89)
	Polymyalgia rheumatica	330	123			2.90 (2.36–3.57)
	Vasculitis	800	444			1.96 (1.74–2.20)
	Psoriasis	1,967	734			2.91 (2.67–3.17)
	Inflammatory bowel disease	7,945	4,863			1.78 (1.72–1.84)
	Celiac disease	434	254			2.68 (2.51–2.85)
Type 1 diabetes mellitus	3,263	1,318			2.68 (2.51–2.85)	
South Korea [120]	Total	177,083	675,750		10.8 months	
	Autoimmune inflammatory rheumatic disease	2,042 (1.15)	5,945 (0.88)			1.25 (1.18–1.31)
	Inflammatory arthritis	56 (0.03)	191 (0.03)			0.90 (0.65–1.24)
	Connective tissue disease	1,999 (1.13)	5,790 (0.86)			1.26 (1.19–1.33)
		Number of events (incidence rate)	Number of events (incidence rate)	Hazard ratio (95% CI)		
South Korea [13]	Total	3,145,388	3,767,039		COVID-19 cohort: 287.6 days	1.11 (1.07–1.15)*
	Alopecia areata	3,301 (13.51)	3,060 (10.43)		Control cohort: 287.7 days	1.24 (1.09–1.42)*
	Alopecia totalis	228 (0.92)	203 (0.68)			1.03 (0.87–1.21)
	Primary cicatricial alopecia	140 (0.57)	158 (0.53)			1.01 (0.96–1.06)
	Psoriasis	1,456 (5.94)	1,791 (6.10)			1.11 (1.04–1.19)*
	Vitiligo	820 (3.32)	896 (3.03)			1.03 (0.79–1.35)
	Sarcoidosis	47 (0.19)	58 (0.20)			1.45 (1.20–1.74)*
	Behçet disease	128 (0.52)	100 (0.34)			

Table 3. Continued

Crohn disease	146 (0.59)	126 (0.42)	1.35 (1.14–1.60)*
Ulcerative colitis	339 (1.37)	332 (1.12)	1.15 (1.04–1.28)*
Rheumatoid arthritis	4,599 (19.13)	5,378 (18.68)	1.09 (1.06–1.12)*
Systemic lupus erythematosus	274 (1.11)	272 (0.92)	1.14 (1.01–1.28)*
Systemic sclerosis	39 (0.16)	51 (0.17)	0.90 (0.67–1.21)
Sjögren syndrome	384 (1.55)	429 (1.45)	1.13 (1.03–1.25)*
Ankylosing spondylitis	542 (2.20)	590 (1.99)	1.11 (1.02–1.20)*
Dermatopolymyositis	47 (0.19)	66 (0.22)	0.84 (0.64–1.09)
Bullous pemphigoid	21 (0.08)	23 (0.08)	1.62 (1.07–2.45)*
Hazard ratio (95% CI)			
Japan [120]			
Total	960,849	1,606,873	11.2 months
Autoimmune inflammatory rheumatic disease	37,168 (3.87)	27,571 (1.72)	1.79 (1.77–1.82)*
Inflammatory arthritis	13,363 (1.39)	8,661 (0.54)	2.02 (1.96–2.07)*
Connective tissue disease	33,261 (3.46)	24,698 (1.54)	1.78 (1.75–1.81)*
Hazard ratio (95% CI)			
Hong Kong [16]			
Total	3,168,131	3,168,467	From index date
Acute disseminated encephalomyelitis	3	10	until death, incident
Alopecia areata	1	8	autoimmune disease,
Anti-phospholipid antibody syndrome	50	76	or study end (1 April
Dermatopolymyositis	24	54	2020–15 November
Graves' disease	204	482	2022), whichever
Guillain barre syndrome	12	37	occurred first
Hashimoto's thyroiditis	11	45	
Immune mediated thrombocytopenia	308	512	
Inflammatory bowel diseases	48	125	
Multiple sclerosis	11	13	
Other autoimmune arthritis	1,028	2,416	
Pemphigoid	95	152	
Pemphigus vulgaris	2	15	
Pernicious anaemia	33	69	
Psoriasis	114	258	
Rheumatoid arthritis	180	473	
Sjogren disease	33	76	
Spondyloarthritis	91	222	

Table 3. Continued

Systemic lupus erythematosus	67	217	1.05 (0.79–1.39)
Systemic sclerosis	14	35	1.20 (0.64–2.25)
Transverse myelitis	5	20	0.77 (0.28–2.09)
Vasculitis	51	118	1.46 (1.04–2.04)*
UK [27]			
Total	458,147	1,818,929	0.29 years (0.24–0.42)
Immune-mediated inflammatory diseases	696 (4.59)	2,230 (3.65)	1.22 (1.12–1.33)*
Autoimmune thyroiditis	< 5 (0.020)	18 (0.029)	0.63 (0.19–2.15)
Celiac disease	37 (0.24)	113 (0.18)	1.30 (0.90–1.89)
Inflammatory bowel diseases	276 (0.18)	817 (0.13)	1.36 (1.18–1.56)*
Myasthenia gravis	5 (0.033)	21 (0.034)	0.92 (0.35–2.45)
Pernicious anaemia	17 (0.11)	50 (0.082)	1.34 (0.77–2.32)
Psoriasis	223 (1.47)	743 (1.22)	1.23 (1.05–1.42)*
Rheumatoid arthritis	66 (0.44)	248 (0.41)	1.06 (0.81–1.40)
Sjogren's syndrome	< 5 (0.00066)	23 (0.038)	0.17 (0.02–1.27)
Systemic lupus erythematosus	10 (0.066)	39 (0.064)	1.02 (0.51–2.05)
Type 1 diabetes mellitus	42 (0.28)	106 (0.17)	1.56 (1.09–2.23)*
Vitiligo	19 (0.13)	60 (0.098)	1.28 (0.77–2.15)
Germany [119]			
Total	641,407	1,907,992	Maximum of 15 months
First onset of autoimmune disease	6,489 (15.05)	4,552 (10.55)	1.43 (1.37–1.48)*
Additional autoimmune disease with preexisting autoimmunity	1,744 (38.1)	1,418 (30.94)	1.23 (1.15–1.32)*
Hashimoto thyroiditis	2,089 (4.41)	1,474 (3.11)	1.42 (1.33–1.52)*
Graves' disease	1,696 (3.52)	1,207 (2.51)	1.41 (1.31–1.51)*
Psoriasis	1,519 (3.17)	1,299 (2.71)	1.17 (1.09–1.26)*
Psoriasis with medication	488 (1)	405 (0.83)	1.21 (1.06–1.38)*
Rheumatoid arthritis	1,175 (2.43)	826 (1.71)	1.42 (1.30–1.56)*
Rheumatoid arthritis with medication	611 (1.26)	421 (0.87)	1.45 (1.28–1.64)*
Sjögren syndrome	604 (1.24)	419 (0.86)	1.44 (1.27–1.63)*
Sjögren syndrome with medication	110 (0.22)	72 (0.15)	1.53 (1.14–2.06)*

Table 3. Continued

Diabetes type 1 with insulin	381 (0.78)	304 (0.62)	1.25 (1.08–1.46)*
Ulcerative colitis	367 (0.75)	282 (0.58)	1.30 (1.12–1.52)*
Ulcerative colitis with medication	212 (0.43)	175 (0.36)	1.22 (1.00–1.49)*
Crohn's disease	298 (0.61)	235 (0.48)	1.27 (1.07–1.50)*
Crohn's disease with medication	155 (0.32)	120 (0.24)	1.29 (1.02–1.64)*
Polymyalgia rheumatica	287 (0.59)	233 (0.47)	1.24 (1.04–1.47)*
Polymyalgia rheumatica with medication	174 (0.36)	154 (0.31)	1.13 (0.91–1.40)
Multiple sclerosis	271 (0.55)	226 (0.46)	1.20 (1.01–1.43)*
Multiple sclerosis with medication	99 (0.2)	96 (0.2)	1.04 (0.78–1.37)
Sarcoidosis	266 (0.54)	124 (0.25)	2.14 (1.73–2.65)*
Ankylosing spondylitis	263 (0.54)	194 (0.4)	1.36 (1.13–1.63)*
Ankylosing spondylitis with medication	82 (0.17)	64 (0.13)	1.29 (0.93–1.78)
Celiac disease	229 (0.47)	148 (0.3)	1.55 (1.26–1.90)*
Alopecia areata	198 (0.4)	152 (0.31)	1.30 (1.05–1.61)*
Vitiligo	132 (0.27)	97 (0.2)	1.36 (1.05–1.77)*
Immune thrombocytopenic purpura	83 (0.17)	53 (0.11)	1.56 (1.10–2.20)*
Immune thrombocytopenic purpura with medication	30 (0.06)	15 (0.03)	1.96 (1.06–3.62)*
Cutaneous lupus erythematosus	81 (0.17)	63 (0.13)	1.29 (0.93–1.80)
Systemic lupus erythematosus	63 (0.13)	47 (0.1)	1.34 (0.92–1.95)
Systemic lupus erythematosus with medication	41 (0.08)	30 (0.06)	1.35 (0.85–2.16)
Arteritis temporalis	53 (0.11)	33 (0.07)	1.63 (1.05–2.53)*
Arteritis temporalis with medication	46 (0.09)	26 (0.05)	1.78 (1.10–2.89)*
Bullous pemphigoid	45 (0.09)	29 (0.06)	1.54 (0.97–2.46)
Myasthenia gravis	41 (0.08)	27 (0.06)	1.5 (0.93–2.44)
Wegener's disease	41 (0.08)	16 (0.03)	2.51 (1.42–4.46)*
Wegener's disease with medication	28 (0.06)	12 (0.03)	2.27 (1.16–4.44)*
Primary biliary cirrhosis	40 (0.08)	32 (0.07)	1.24 (0.78–1.97)
Autoimmune hepatitis	38 (0.08)	35 (0.07)	1.10 (0.69–1.74)
Systemic sclerosis	35 (0.07)	50 (0.1)	0.70 (0.45–1.08)
Autoimmune hemolytic anemia	21 (0.04)	15 (0.03)	1.37 (0.71–2.65)
Behcet's disease	21 (0.04)	9 (0.02)	2.42 (1.10–5.35)*
Guillain-Barré syndrome	20 (0.04)	9 (0.02)	2.14 (0.99–4.66)

CI, confidence interval; UK, United Kingdom; US, United States; PY, person-year.

^aThe reported cohort population represents the sample size after propensity score matching.

*Indicates a statistically significant.

risks associated with different SARS-CoV-2 strains, including Delta and Omicron, remain insufficiently characterized [16]. Each variant exhibits distinct biological behavior, pathogenicity, and clinical impact [122]. Inconsistencies in diagnostic criteria and the limited range of autoimmune diseases examined further constrain the interpretability and comprehensiveness of current findings. Finally, reliance on hospital-based cohorts may introduce selection bias by disproportionately representing more severe cases [5].

Addressing these challenges requires several strategic approaches. First, long-term, multinational prospective cohorts should be established to monitor the incidence of post-COVID-19 autoimmune diseases. Inclusion of populations from low- and middle-income countries is essential, since differences in healthcare access and baseline comorbidities may result in distinct autoimmune risk patterns following long COVID. International collaboration and open-data initiatives should be promoted to enable comprehensive analyses and rapid dissemination of findings. Second, longitudinal tracking of clinical outcomes and immune markers is needed, with particular emphasis on variant-specific effects, vaccination status, and associations with disease severity. Third, personalized risk stratification models integrating clinical, genetic, and immunological markers should be developed to identify individuals at increased risk of post-COVID-19 autoimmune conditions. Fourth, the impact of vaccination strategies and booster protocols on reducing autoimmune risk should be systematically evaluated. Overall, recognizing autoimmune diseases as a part of the post-acute sequelae of SARS-CoV-2 infection requires a coordinated and multidisciplinary approach that integrates mechanistic research, longitudinal clinical studies, personalized risk assessment, and therapeutic development.

COVID-19 VACCINATION AND AUTOIMMUNE RHEUMATIC DISEASE

Reports have described the development of autoimmune diseases, including Graves' disease, autoimmune liver disease, GBS, RA, type 1 diabetes, and SLE, following COVID-19 vaccination, suggesting a potential association [123-126]. However, such case reports are insufficient to establish causality. A nationwide, population-based cohort study in Korea found no significant association between mRNA vaccination and most autoimmune diseases [18]. However, increased

risks were observed for specific conditions, including SLE, myocarditis, pericarditis [127], and GBS, compared with a historical control cohort [18]. However, another study using the same dataset found that the risk of autoimmune diseases following SARS-CoV-2 infection was significantly lower among vaccinated individuals than among unvaccinated individuals (HR, 0.59 after one dose and 0.42 after two doses) [120]. Similar results were reported in a retrospective cohort study conducted in Hong Kong, which showed that vaccination was associated with reduced risks of autoimmune diseases, including Graves' disease and SLE, among patients with COVID-19 [16]. These findings suggest the potential protective effect of vaccination against the development of autoimmune diseases during the COVID-19 pandemic. Given the favorable safety profile of vaccines in this context and their established role in reducing SARS-CoV-2-related morbidity and mortality, vaccination remains a key public health strategy.

CONCLUSION

The bidirectional relationship between COVID-19 and autoimmune diseases has important clinical and immunological implications. Individuals with autoimmune diseases are at increased risk of infection and severe outcomes due to underlying immune dysregulation and the use of immunosuppressive therapies. Conversely, SARS-CoV-2 infection can trigger the onset or exacerbation of autoimmune diseases through mechanisms such as molecular mimicry, bystander activation, and sustained immune activation. These findings highlight the need for individualized patient management, including careful adjustment of immunosuppressive therapy, optimization of vaccination timing, and close monitoring of disease activity and vaccine responses. Future research should focus on elucidating the long-term outcomes of post-COVID-19 autoimmune manifestations and ensuring the continued safety and effectiveness of vaccines in immunocompromised populations. A deeper understanding of these complex interactions will be essential to improving clinical care, informing treatment strategies, and enhancing preparedness for future pandemics involving immune-mediated diseases.

REFERENCES

- GBD 2021 Demographics Collaborators. Global age-sex-specific mortality, life expectancy, and population estimates in 204 countries and territories and 811 subnational locations, 1950-2021, and the impact of the COVID-19 pandemic: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. *Lancet* 2024;403:1989-2056.
- Lee S, Hwang SH, Park S, et al. Burden of cardiovascular outcomes after SARS-CoV-2 infection in South Korea and Japan: a binational population-based cohort study. *Circulation* 2025;152:11-23.
- Harris E. COVID-19 associated with higher risk of autoimmune diseases. *JAMA* 2024;331:1266.
- Cao F, He YS, Wang Y, et al. Global burden and cross-country inequalities in autoimmune diseases from 1990 to 2019. *Autoimmun Rev* 2023;22:103326.
- Chang R, Yen-Ting Chen T, Wang SI, Hung YM, Chen HY, Wei CJ. Risk of autoimmune diseases in patients with COVID-19: a retrospective cohort study. *EClinicalMedicine* 2023;56:101783.
- Pisetsky DS. Pathogenesis of autoimmune disease. *Nat Rev Nephrol* 2023;19:509-524.
- Lamers MM, Haagmans BL. SARS-CoV-2 pathogenesis. *Nat Rev Microbiol* 2022;20:270-284.
- Klein J, Wood J, Jaycox JR, et al. Distinguishing features of long COVID identified through immune profiling. *Nature* 2023;623:139-148.
- Ruhl L, Pink I, Kühne JF, et al. Endothelial dysfunction contributes to severe COVID-19 in combination with dysregulated lymphocyte responses and cytokine networks. *Signal Transduct Target Ther* 2021;6:418.
- Sen P, R N, Nune A, et al. Post-COVID-19 condition in patients with autoimmune rheumatic diseases: the COVID-19 vaccination in autoimmune diseases (COVAD) study. *Lancet Rheumatol* 2023;5:e247-e250.
- Gianfrancesco M, Hyrich KL, Al-Adely S, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 global rheumatology alliance physician-reported registry. *Ann Rheum Dis* 2020;79:859-866.
- Shin YH, Shin JI, Moon SY, et al. Autoimmune inflammatory rheumatic diseases and COVID-19 outcomes in South Korea: a nationwide cohort study. *Lancet Rheumatol* 2021;3:e698-e706.
- Heo YW, Jeon JJ, Ha MC, Kim YH, Lee S. Long-term risk of autoimmune and autoinflammatory connective tissue disorders following COVID-19. *JAMA Dermatol* 2024;160:1278-1287.
- Phetsouphanh C, Darley DR, Wilson DB, et al. Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. *Nat Immunol* 2022;23:210-216.
- Shah S, Danda D, Kavadiachanda C, Das S, Adarsh MB, Negi VS. Autoimmune and rheumatic musculoskeletal diseases as a consequence of SARS-CoV-2 infection and its treatment. *Rheumatol Int* 2020;40:1539-1554.
- Peng K, Li X, Yang D, et al. Risk of autoimmune diseases following COVID-19 and the potential protective effect from vaccination: a population-based cohort study. *eClinicalMedicine* 2023;63:102154.
- Boekel L, Steenhuis M, Hooijberg F, et al. Antibody development after COVID-19 vaccination in patients with autoimmune diseases in the Netherlands: a substudy of data from two prospective cohort studies. *Lancet Rheumatol* 2021;3:e778-e788.
- Jung SW, Jeon JJ, Kim YH, Choe SJ, Lee S. Long-term risk of autoimmune diseases after mRNA-based SARS-CoV2 vaccination in a Korean, nationwide, population-based cohort study. *Nat Commun* 2024;15:6181.
- Al-Janabi A, Littlewood Z, Griffiths CEM, et al. Antibody responses to single-dose SARS-CoV-2 vaccination in patients receiving immunomodulators for immune-mediated inflammatory disease. *Br J Dermatol* 2021;185:646-648.
- Gianfrancesco MA, Hyrich KL, Gossec L, et al. Rheumatic disease and COVID-19: initial data from the COVID-19 global rheumatology alliance provider registries. *Lancet Rheumatol* 2020;2:e250-e253.
- Gusev E, Sarapultsev A, Solomatina L, Chereshev V. SARS-CoV-2-specific immune response and the pathogenesis of COVID-19. *Int J Mol Sci* 2022;23:1716.
- Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-1034.
- Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis* 2020;71:762-768.
- Kourbeti IS, Ziakas PD, Mylonakis E. Biologic therapies in rheumatoid arthritis and the risk of opportunistic infections: a meta-analysis. *Clin Infect Dis* 2014;58:1649-1657.
- Brenner EJ, Ungaro RC, Gearry RB, et al. Corticosteroids, but not TNF antagonists, are associated with adverse COVID-19 outcomes in patients with inflammatory bowel diseases:

- results from an international registry. *Gastroenterology* 2020;159:481-491.e3.
26. Singh N, Madhira V, Hu C, et al. Rituximab is associated with worse COVID-19 outcomes in patients with rheumatoid arthritis: a retrospective, nationally sampled cohort study from the U.S. National COVID Cohort Collaborative (N3C). *Semin Arthritis Rheum* 2023;58:152149.
 27. Syed U, Subramanian A, Wraith DC, et al. Incidence of immune-mediated inflammatory diseases following COVID-19: a matched cohort study in UK primary care. *BMC Med* 2023;21:363.
 28. Bastard P, Rosen LB, Zhang Q, et al. Autoantibodies against type I IFNs in patients with life-threatening COVID-19. *Science* 2020;370:eabd4585.
 29. Zuo Y, Estes SK, Ali RA, et al. Prothrombotic autoantibodies in serum from patients hospitalized with COVID-19. *Sci Transl Med* 2020;12:eabd3876.
 30. Zhou Y, Han T, Chen J, et al. Clinical and autoimmune characteristics of severe and critical cases of COVID-19. *Clin Transl Sci* 2020;13:1077-1086.
 31. Vojdani A, Kharrazian D. Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. *Clin Immunol* 2020;217:108480.
 32. Gazzaruso C, Carlo Stella N, Mariani G, et al. High prevalence of antinuclear antibodies and lupus anticoagulant in patients hospitalized for SARS-CoV2 pneumonia. *Clin Rheumatol* 2020;39:2095-2097.
 33. Mohkhedkar M, Venigalla SSK, Janakiraman V. Untangling COVID-19 and autoimmunity: Identification of plausible targets suggests multi organ involvement. *Mol Immunol* 2021;137:105-113.
 34. Sharma C, Bayry J. High risk of autoimmune diseases after COVID-19. *Nat Rev Rheumatol* 2023;19:399-400.
 35. Kim HJ, Kim MH, Park SJ, Choi MG, Chun EM. Autoimmune adverse event following COVID-19 vaccination in Seoul, South Korea. *J Allergy Clin Immunol* 2024;153:1711-1720.
 36. Ferri C, Ursini F, Gragnani L, et al. Impaired immunogenicity to COVID-19 vaccines in autoimmune systemic diseases. High prevalence of non-response in different patients' subgroups. *J Autoimmun* 2021;125:102744.
 37. Lee ARYB, Wong SY, Chai LYA, et al. Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis. *BMJ* 2022;376:e068632.
 38. Wroński J, Ciechomska M, Kuca-Warnawin E. Impact of methotrexate treatment on vaccines immunogenicity in adult rheumatological patients - lessons learned from the COVID-19 pandemic. *Biomed Pharmacother* 2023;165:115254.
 39. Smolen JS, Landewé RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. *Ann Rheum Dis* 2023;82:3-18.
 40. Haberman RH, Herati R, Simon D, et al. Methotrexate hampers immunogenicity to BNT162b2 mRNA COVID-19 vaccine in immune-mediated inflammatory disease. *Ann Rheum Dis* 2021;80:1339-1344.
 41. Mahil SK, Bechman K, Raharja A, et al. The effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses to the COVID-19 vaccine BNT162b2: a cohort study. *Lancet Rheumatol* 2021;3:e627-e637.
 42. Oliosi E, Flahault A, Charre C, et al. Impact of rituximab on humoral response to SARS-CoV-2 vaccination in previously vaccinated patients with autoimmune diseases. *Clin Rheumatol* 2023;42:2485-2490.
 43. Furer V, Eviatar T, Zisman D, et al. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases and in the general population: a multicentre study. *Ann Rheum Dis* 2021;80:1330-1338.
 44. Iancovici L, Khateeb D, Harel O, et al. Rheumatoid arthritis patients treated with Janus kinase inhibitors show reduced humoral immune responses following BNT162b2 vaccination. *Rheumatology (Oxford)* 2022;61:3439-3447.
 45. Dudley HM, O'Mara M, Auma A, et al. Rheumatoid arthritis and older age are associated with lower humoral and cellular immune response to primary series COVID-19 mRNA vaccine. *Vaccine* 2023;41:6112-6119.
 46. Sparks JA, Wallace ZS, Seet AM, et al. Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: results from the COVID-19 global rheumatology alliance physician registry. *Ann Rheum Dis* 2021;80:1137-1146.
 47. Abhishek A, Peckham N, Pade C, et al. Effect of a 2-week interruption in methotrexate treatment on COVID-19 vaccine response in people with immune-mediated inflammatory diseases (VROOM study): a randomised, open label, superiority trial. *Lancet Rheumatol* 2024;6:e92-e104.
 48. Schultz K, Jannat-Khah D, Spiera R. B cell reconstitution is associated with COVID-19 booster vaccine responsiveness in patients previously seronegative treated with rituximab. *J Rheumatol* 2023;50:420-425.

49. Hanberg JS, Fu X, Wang X, et al. Effectiveness of a fourth dose of COVID-19 mRNA vaccine in patients with systemic autoimmune rheumatic diseases using disease-modifying antirheumatic drugs: an emulated target trial. *Lancet Rheumatol* 2024;6:e21-e30.
50. Hoi A, Igel T, Mok CC, Arnaud L. Systemic lupus erythematosus. *Lancet* 2024;403:2326-2338.
51. Siegel CH, Sammaritano LR. Systemic lupus erythematosus: a review. *JAMA* 2024;331:1480-1491.
52. Mageau A, G  radin C, Sallah K, Papo T, Sacre K, Timsit JF. Risk of systemic lupus erythematosus flare after COVID-19 hospitalization: a matched cohort study. *PLoS One* 2024;19:e0309316.
53. Ugarte-Gil MF, Alarc  n GS, Izadi Z, et al. Characteristics associated with poor COVID-19 outcomes in individuals with systemic lupus erythematosus: data from the COVID-19 global rheumatology alliance. *Ann Rheum Dis* 2022;81:970-978.
54. Mehta P, Gasparyan AY, Zimba O, Kitas GD. Systemic lupus erythematosus in the light of the COVID-19 pandemic: infection, vaccination, and impact on disease management. *Clin Rheumatol* 2022;41:2893-2910.
55. Yang F, Zhang N, Meng R, et al. Non-causal association of COVID-19 with systemic lupus erythematosus: evidence from a bidirectional Mendelian randomization. *J Infect* 2023;86:e87-e90.
56. Felten R, Kawka L, Dubois M, et al. Tolerance of COVID-19 vaccination in patients with systemic lupus erythematosus: the international VACOLUP study. *Lancet Rheumatol* 2021;3:e613-e615.
57. Pappa M, Panagiotopoulos A, Thomas K, Fanouriakis A. Systemic lupus erythematosus and COVID-19. *Curr Rheumatol Rep* 2023;25:192-203.
58. Petri M, Joyce D, Haag K, et al. Effect of Systemic lupus erythematosus and immunosuppressive agents on COVID-19 vaccination antibody response. *Arthritis Care Res (Hoboken)* 2023;75:1878-1885.
59. Tan SYS, Yee AM, Sim JLL, Lim CC. COVID-19 vaccination in systemic lupus erythematosus: a systematic review of its effectiveness, immunogenicity, flares and acceptance. *Rheumatology (Oxford)* 2023;62:1757-1772.
60. Di Matteo A, Bathon JM, Emery P. Rheumatoid arthritis. *Lancet* 2023;402:2019-2033.
61. Yadav S, Bonnes SL, Gilman EA, et al. Inflammatory arthritis after COVID-19: a case series. *Am J Case Rep* 2023;24:e939870.
62. Mar  n JS, Mazonett-Granados EA, Salazar-Uribe JC, et al. Increased incidence of rheumatoid arthritis after COVID-19. *Autoimmun Rev* 2023;22:103409.
63. D'Silva KM, Jorge A, Cohen A, et al. COVID-19 outcomes in patients with systemic autoimmune rheumatic diseases compared to the general population: a US multicenter, comparative cohort study. *Arthritis Rheumatol* 2021;73:914-920.
64. Wang Y, D'Silva KM, Jorge AM, et al. Increased risk of COVID-19 in patients with rheumatoid arthritis: a general population-based cohort study. *Arthritis Care Res (Hoboken)* 2022;74:741-747.
65. Li H, Wallace ZS, Sparks JA, et al. Risk of COVID-19 among unvaccinated and vaccinated patients with rheumatoid arthritis: a general population study. *Arthritis Care Res (Hoboken)* 2023;75:956-966.
66. Figueroa-Parra G, Gilbert EL, Valenzuela-Almada MO, et al. Risk of severe COVID-19 outcomes associated with rheumatoid arthritis and phenotypic subgroups: a retrospective, comparative, multicentre cohort study. *Lancet Rheumatol* 2022;4:e765-e774.
67. Cordtz R, Kristensen S, Westermann R, et al. COVID-19 infection and hospitalization risk according to vaccination status and DMARD treatment in patients with rheumatoid arthritis. *Rheumatology (Oxford)* 2022;62:77-88.
68. Naveen R, Parodis I, Joshi M, et al. COVID-19 vaccination in autoimmune diseases (COVAD) study: vaccine safety and tolerance in rheumatoid arthritis. *Rheumatology (Oxford)* 2023;62:2366-2376.
69.   lvarez-Gracia JM, Sanchez-Piedra C, Culqui D, et al. Effects of COVID-19 vaccination on disease activity in patients with rheumatoid arthritis and psoriatic arthritis on targeted therapy in the COVIDSER study. *RMD Open* 2023;9:e002936.
70. Strangfeld A, Sch  fer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 global rheumatology alliance physician-reported registry. *Ann Rheum Dis* 2021;80:930-942.
71. GBD 2021 Rheumatoid Arthritis Collaborators. Global, regional, and national burden of rheumatoid arthritis, 1990-2020, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. *Lancet Rheumatol* 2023;5:e594-e610.
72. GBD 2023 Causes of Death Collaborators. Global burden of 292 causes of death in 204 countries and territories and 660 subnational locations, 1990-2023: a systematic analysis for the Global Burden of Disease Study 2023. *Lancet*

- 2025;406:1811-1872.
73. GBD 2023 Disease and Injury and Risk Factor Collaborators. Burden of 375 diseases and injuries, risk-attributable burden of 88 risk factors, and healthy life expectancy in 204 countries and territories, including 660 subnational locations, 1990-2023: a systematic analysis for the Global Burden of Disease Study 2023. *Lancet* 2025;406:1873-1922.
 74. GBD 2023 Demographics Collaborators. Global age-sex-specific all-cause mortality and life expectancy estimates for 204 countries and territories and 660 subnational locations, 1950-2023: a demographic analysis for the Global Burden of Disease Study 2023. *Lancet* 2025;406:1731-1810.
 75. Jakimovski D, Bittner S, Zivadinov R, et al. Multiple sclerosis. *Lancet* 2024;403:183-202.
 76. Bjornevik K, Cortese M, Healy BC, et al. Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis. *Science* 2022;375:296-301.
 77. Bsteh G, Assar H, Gradl C, et al. Long-term outcome after COVID-19 infection in multiple sclerosis: a nation-wide multicenter matched-control study. *Eur J Neurol* 2022;29:3050-3060.
 78. Montini F, Nozzolillo A, Tedone N, et al. COVID-19 has no impact on disease activity, progression and cognitive performance in people with multiple sclerosis: a 2-year study. *J Neurol Neurosurg Psychiatry* 2024;95:342-347.
 79. Rahmani M, Moghadasi AN, Shahi S, et al. COVID-19 and its implications on the clinico-radiological course of multiple sclerosis: a case-control study. *Med Clin (Engl Ed)* 2023;160:187-192.
 80. Peeters G, Van Remoortel A, Nagels G, Van Schependom J, D'Haeseleer M. Occurrence and severity of coronavirus disease 2019 are associated with clinical disability worsening in patients with multiple sclerosis. *Neurol Neuroimmunol Neuroinflamm* 2023;10:e200089.
 81. Prosperini L, Arrambide G, Celius EG, et al. COVID-19 and multiple sclerosis: challenges and lessons for patient care. *Lancet Reg Health Eur* 2024;44:100979.
 82. Sormani MP, Schiavetti I, Carmisciano L, et al. COVID-19 severity in multiple sclerosis: putting data into context. *Neurol Neuroimmunol Neuroinflamm* 2022;9:e1105.
 83. Simpson-Yap S, Pirmani A, Kalincik T, et al. Updated results of the COVID-19 in MS global data sharing initiative: anti-CD20 and other risk factors associated with COVID-19 severity. *Neurol Neuroimmunol Neuroinflamm* 2022;9:e200021.
 84. Januel E, Hajage D, Labauge P, et al. Association between anti-CD20 therapies and COVID-19 severity among patients with relapsing-remitting and progressive multiple sclerosis. *JAMA Netw Open* 2023;6:e2319766.
 85. Baranova A, Cao H, Teng S, Su KP, Zhang F. Shared genetics and causal associations between COVID-19 and multiple sclerosis. *J Med Virol* 2023;95:e28431.
 86. Sormani MP, De Rossi N, Schiavetti I, et al. Disease-modifying therapies and coronavirus disease 2019 severity in multiple sclerosis. *Ann Neurol* 2021;89:780-789.
 87. Sormani MP, Salvetti M, Labauge P, et al. DMTs and Covid-19 severity in MS: a pooled analysis from Italy and France. *Ann Clin Transl Neurol* 2021;8:1738-1744.
 88. Zabalza A, Thompson A, Rotstein DL, Bar-Or A, Montalban X. Multiple sclerosis and COVID-19: interactions and unresolved issues. *Lancet Neurol* 2025;24:361-370.
 89. GBD 2016 Multiple Sclerosis Collaborators. Global, regional, and national burden of multiple sclerosis 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;18:269-285.
 90. GBD 2017 Inflammatory Bowel Disease Collaborators. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol* 2020;5:17-30.
 91. Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019;68(Suppl 3):s1-s106.
 92. Lim SH, Ju HJ, Han JH, et al. Autoimmune and autoinflammatory connective tissue disorders following COVID-19. *JAMA Netw Open* 2023;6:e2336120.
 93. Imperatore N, Bennato R, D'Avino A, Lombardi G, Manguso F. SARS-CoV-2 as a trigger for de novo ulcerative colitis. *Inflamm Bowel Dis* 2021;27:e87-e88.
 94. Taxonera C, Fisac J, Alba C. Can COVID-19 trigger de novo inflammatory bowel disease? *Gastroenterology* 2021;160:1029-1030.
 95. Tursi A, Nenna R. COVID-19 as a trigger for de novo Crohn's disease. *Inflamm Bowel Dis* 2022;28:e76-e77.
 96. Calabrese E, Zorzi F, Monteleone G, Del Vecchio Blanco G. Onset of ulcerative colitis during SARS-CoV-2 infection. *Dig Liver Dis* 2020;52:1228-1229.
 97. Lee MH, Li HJ, Wasuwanich P, et al. COVID-19 susceptibility and clinical outcomes in inflammatory bowel disease: an updated systematic review and meta-analysis. *Rev Med Virol* 2023;33:e2414.
 98. Lutz M, Lazarus S, Caldera F. COVID-19 vaccination in adults

- with inflammatory bowel disease. *Ther Adv Gastroenterol* 2023;16:17562848231173130.
99. Macaluso FS, Giuliano A, Fries W, et al. Severe activity of inflammatory bowel disease is a risk factor for severe COVID-19. *Inflamm Bowel Dis* 2023;29:217-221.
100. Card TR, Nakafero G, Grainge MJ, et al. Is vaccination against COVID-19 associated with inflammatory bowel disease flare? Self-controlled case series analysis using the UK CPRD. *Am J Gastroenterol* 2023;118:1388-1394.
101. Dou D, Zhang F, Deng X, et al. Efficacy of COVID-19 vaccines in inflammatory bowel disease patients receiving anti-TNF therapy: a systematic review and meta-analysis. *Heliyon* 2023;9:e19609.
102. Peng YL, Chang CH, Wei SC, et al. Impact of the COVID-19 pandemic on inflammatory bowel disease care in Taiwan: a multicenter study. *J Formos Med Assoc* 2023;122:1042-1049.
103. Abdulla M, Mohammed N, AlQamish J, Mosli M. Inflammatory bowel disease and COVID-19 outcomes: a meta-analysis. *Sci Rep* 2022;12:21333.
104. Shahrazaila N, Lehmann HC, Kuwabara S. Guillain-Barré syndrome. *Lancet* 2021;397:1214-1228.
105. Jeong YD, Park S, Lee S, et al. Global burden of vaccine-associated Guillain-Barré syndrome over 170 countries from 1967 to 2023. *Sci Rep* 2024;14:24561.
106. Leonhard SE, Mandarakas MR, Gondim FAA, et al. Diagnosis and management of Guillain-Barré syndrome in ten steps. *Nat Rev Neurol* 2019;15:671-683.
107. Toscano G, Palmerini F, Ravaglia S, et al. Guillain-Barré syndrome associated with SARS-CoV-2. *N Engl J Med* 2020;382:2574-2576.
108. Filosto M, Cotti Piccinelli S, Gazzina S, et al. Guillain-Barré syndrome and COVID-19: a 1-year observational multicenter study. *Eur J Neurol* 2022;29:3358-3367.
109. Xu E, Xie Y, Al-Aly Z. Long-term neurologic outcomes of COVID-19. *Nat Med* 2022;28:2406-2415.
110. Bishara H, Arbel A, Barnett-Griness O, et al. Association between Guillain-Barré syndrome and COVID-19 infection and vaccination: a population-based nested case-control study. *Neurology* 2023;101:e2035-e2042.
111. Hussain FS, Eldeeb MA, Blackmore D, Siddiqi ZA. Guillain Barré syndrome and COVID-19: possible role of the cytokine storm. *Autoimmun Rev* 2020;19:102681.
112. Abara WE, Gee J, Marquez P, et al. Reports of Guillain-Barré syndrome after COVID-19 vaccination in the United States. *JAMA Netw Open* 2023;6:e2253845.
113. Le Vu S, Bertrand M, Botton J, et al. Risk of Guillain-Barré syndrome following COVID-19 vaccines: a nationwide self-controlled case series study. *Neurology* 2023;101:e2094-e2102.
114. Pegat A, Vogrig A, Khouri C, Masmoudi K, Vial T, Bernard E. Adenovirus COVID-19 vaccines and Guillain-Barré syndrome with facial paralysis. *Ann Neurol* 2022;91:162-163.
115. Finsterer J, Scorza FA, Scorza CA. Guillain-Barré syndrome associated with COVID-19 vaccination. *Emerg Infect Dis* 2022;28:1079-1080.
116. Meo SA, Shaikh N, Abukhalaf FA, Meo AS. Exploring the adverse events of Oxford-AstraZeneca, Pfizer-BioNTech, Moderna, and Johnson and Johnson COVID-19 vaccination on Guillain-Barré syndrome. *Sci Rep* 2024;14:18767.
117. Lazear HM, Schoggins JW, Diamond MS. Shared and distinct functions of type I and type III interferons. *Immunity* 2019;50:907-923.
118. Bieber A, Sagy I, Novack L, et al. BNT162b2 mRNA COVID-19 vaccine and booster in patients with autoimmune rheumatic diseases: a national cohort study. *Ann Rheum Dis* 2022;81:1028-1035.
119. Carlile O, Briggs A, Henderson AD, et al. Impact of long COVID on health-related quality-of-life: an OpenSAFE-LY population cohort study using patient-reported outcome measures (OpenPROMPT). *Lancet Reg Health Eur* 2024;40:100908.
120. Kim MS, Lee H, Lee SW, et al. Long-term autoimmune inflammatory rheumatic outcomes of COVID-19 : a binational cohort study. *Ann Intern Med* 2024;177:291-302.
121. Tesch F, Ehm F, Vivirito A, et al. Incident autoimmune diseases in association with SARS-CoV-2 infection: a matched cohort study. *Clin Rheumatol* 2023;42:2905-2914.
122. Sun K, Bhiman JN, Tempia S, et al. SARS-CoV-2 correlates of protection from infection against variants of concern. *Nat Med* 2024;30:2805-2812.
123. Chen Y, Xu Z, Wang P, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. *Immunology* 2022;165:386-401.
124. Guo M, Liu X, Chen X, Li Q. Insights into new-onset autoimmune diseases after COVID-19 vaccination. *Autoimmun Rev* 2023;22:103340.
125. Safary A, Esalatmanesh K, Eftekharsadat AT, Jafari Nakjavani MR, Khabbazi A. Autoimmune inflammatory rheumatic diseases post-COVID-19 vaccination. *Int Immunopharmacol* 2022;110:109061.
126. Bostan H, Ucan B, Kizilgul M, et al. Relapsed and newly diagnosed Graves' disease due to immunization against

COVID-19: a case series and review of the literature. *J Autoimmun* 2022;128:102809.

127. Lee S, Jo H, Lee H, et al. Global estimates on the reports of vaccine-associated myocarditis and pericarditis from 1969 to 2023: findings with critical reanalysis from the WHO pharmacovigilance database. *J Med Virol* 2024;96:e29693.

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The authors disclose no conflicts.

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