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# The changes in global burden of autoimmune diseases two years after the COVID-19 pandemic: a trend analysis based on the Global Burden of Disease Study 2021

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ABSTRACT

*Background:* Data on the epidemiological changes in the global burden of autoimmune diseases (ADs) after the Coronavirus disease 2019 (COVID-19) pandemic is lacking. This study investigated the impact of the COVID-19 pandemic on the global burden of ADs, including psoriasis (PsO), inflammatory bowel disease (IBD), type 1 diabetes (T1DM), rheumatoid arthritis (RA), and multiple sclerosis (MS).

*Methods:* Age-standardized rates (ASR), including incidence (ASIR), prevalence (ASPR), disability-adjusted life years (DALYs), and death (ASDR), were extracted from the Global Burden of Disease Study 2021 from 1990 to 2021. The changes in number and ASR of ADs burden were assessed by absolute and relative increases comparing 2021 to 2019. Joinpoint regression analysis was used to determine whether the year 2019 marked the substantial changes in trends of ASR across global, 21 geographical regions, and 204 countries. The correlations between COVID-19 incidence, vaccination and the relative increased ASIR/ASPR of ADs were also evaluated.

*Results:* Joinpoint regression analysis identified 2019 as a pivotal year, marking a global increase in the burden of PsO. The global ASR of PsO in 2021 showed an increased incidence, prevalence, and DALYs of 0.78, 5, and 0.33 DALYs per 100,000, respectively, compared to 2019 ($194.1 \times 10^3$ cases, $1651.3 \times 10^3$ cases, and $131.4 \times 10^3$ DALYs, respectively). Notable absolute increases in PsO incidence rates in 2021 were observed in regions with a high socio-demographic index, particularly among individuals aged 50 to 54 and among males. Furthermore, 2019 marked a joinpoint with increased ASIR or ASPR of ADs in various regions, notably PsO in High-income North America, Southern Latin America, and South Asia, as well as IBD in Southern and Eastern Sub-Saharan Africa, Central Europe, and East Asia. Regional data from the USA, England, and Japan indicated a positive correlation between COVID-19 incidence and relative increases in the burden of PsO in 2020 (Spearman R 0.35, 0.24, and 0.36, respectively, for incidence; R 0.35, 0.2, and 0.36, respectively, for prevalence; all $p < 0.05$). Additionally, 2021 state-level vaccination rates in the USA were negatively correlated with the relative increases in the ASIR of PsO and RA (R: 0.27 and −0.54, respectively; $p < 0.001$ for all), as well as the ASPR of PsO, RA, and MS (R: 0.45, −0.49, and −0.41, respectively; $p < 0.01$ for all) in 2021.

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*Conclusions:* The year 2019 marked a pivotal point for increased global burden of PsO and regional burdens of other ADs. These observations have important implications for subsequent healthcare planning and resource allocation.

## 1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, which caused the Coronavirus disease 2019 (COVID-19) pandemic since December 2019, is associated with various upper and lower respiratory tract problems as well as systemic complications in different organs [1]. Patients infected with COVID-19 may also experience "long COVID syndrome", characterized by symptoms persisting beyond the initially affected organs [1]. In particular, the evolving burden of autoimmune diseases (ADs) post-pandemic is of urgent concern, necessitating comprehensive epidemiological studies to understand changes in the overall burden of ADs. On one hand, patients with ADs have shown an increased risk of COVID-19 infection and mortality [2]; on the other hand, the SARS-CoV-2 virus can trigger aberrant immune responses to autoimmunity [3–8]. To complicate the matter further, while COVID-19 vaccines showed proven benefits in reducing serious complications and mortality in infected subjects and are recommended for patients with ADs, there are concerns that these vaccines may trigger or exacerbate autoimmune conditions [9–11]. Additionally, treatment disruption due to the collapse of the health system may also raise risks of relapses of ADs [12]. Examples of these ADs include psoriasis (PsO), inflammatory bowel disease (IBD), type 1 diabetes mellitus (T1DM), rheumatoid arthritis (RA), and multiple sclerosis (MS), which affect more than ten million of individuals globally and impose significant healthcare and economic burdens on society [13,14]. Most of the existing data on changes in disease burden originate from retrospective studies conducted within a single country or territory [8,12,15]. Therefore, their generalizability is significantly influenced by the clinical epidemiology and healthcare infrastructure unique to each nation. It remains largely unknown whether the COVID-19 pandemic has exerted a profound impact on the epidemiological changes in the burden of autoimmune diseases across different regions, countries, and age groups.

The Global Burden of Disease Study (GBD) 2021 [16,17] serves as an essential resource for evaluating health challenges by location, age, gender, and different SDI (socio-demographic index). In this research, we aimed to identify if 2019 marked a pivotal year indicating upward trends for PsO, IBD, T1DM, RA, and MS. Additionally, we investigated the relationship between COVID-19 incidence, vaccination, and shifts in the burden of these diseases. The data will help refine current strategies for monitoring the ADs as a part of "Long COVID" management in the post-COVID-19 era and assist healthcare service planning.

## 2. Methods

### 2.1. Data acquisition

The GBD 2021 study [16,17] reported estimates with 95 % uncertainty intervals (UI) of incidence, prevalence, mortality, and Disability-Adjusted Life Years (DALYs) from 1990 to 2021 for five ADs (PsO, IBD, T1DM, RA, and MS). (Supplementary methods) This data is available globally, as well as across 5 SDI regions, 21 geographical regions, and 204 countries and territories. Mortality data for PsO were unavailable. The metrics for each burden included the number, age-specific crude rate, and age-standardized rate (ASR, per 100,000 population). ASR metrics cover age-standardized incidence rates (ASIR), prevalence rates (ASPR), DALY rates (ASDR), and mortality rates (ASMR). For the correlation analysis described below, data on ADs and the COVID-19 burden were extracted from 51 states in the United States of America (USA), 150 districts in England, and 47 prefectures in Japan, as documented in GBD 2021.Vaccination data for the USA at the state level was collected from Our World in Data (OWID, available at https://ourworldindata.org/covid-vaccinations), as documented by Mathieu, E. et al. [18]. The vaccination rate is defined as the number of individuals who have received at least one vaccine dose per 100 people [18].

### 2.2. Data analysis

The primary objective of this study was to determine if the year 2019 marked significant alterations in trends of disease burden of ADs, specifically ASIR, ASPR, and ASDR from 1990 to 2021, via joinpoint regression analysis [19]. To begin, a log-linear model was employed for segmented regression analysis of the dataset. We applied the grid search method to identify potential joinpoints by assessing the mean squared error for each possible scenario and selecting the joinpoint corresponding to the minimum error. The optimal joinpoint regression model was established through the Monte Carlo permutation test, with a capacity for up to five joinpoints. The annual percent change (APC) with a 95 % confidence interval (CI) for each identified trend was calculated using the regression formula: $y = \alpha + \beta x + \varepsilon$, where y represents ln (ASR), x represents the calendar year, and ε is an error term. Subsequently, the APC was calculated using the formula: $APC = 100 \times (e^{\beta} - 1)$. The average annual percent change (AAPC), a weighted average of the APCs of all the APCs in the trend analysis, was also calculated. The statistical significance of APCs and AAPCs in comparison to the null hypothesis (slope = 0) and inter-group differences was evaluated (significance level $p < 0.05$).

The second objective was to demonstrate the precise increased burden following the COVID-19 pandemic by calculating the absolute and relative differences in ASR and case numbers comparing values from 2020/2021 to 2019. ASR of disease burden was used as it allows for comparison of event rates among populations with different age structures. The absolute difference for post-COVID-19 years relative to 2019 is defined as the ASR/cases in 2020/2021 minus the ASR/cases in 2019 for specific sexes, causes, and locations. The relative difference, expressed as a difference in percentage, was calculated by dividing the absolute difference by the corresponding ASR/cases in 2019 and then multiplying by 100. Here, a positive value implies that the absolute or relative difference in 2020/2021 exceeds that of 2019.

The third objective focused on identifying the change in disease burden post-pandemic across 20 age groups. The absolute age-specific difference rate is the rate in 2021 minus the rate in 2019 for a specific age group, where a positive value denotes an increase in the crude rate for 2021 compared to 2019.

The fourth objective was to assess whether the drivers of changes in the burden of ADs have shifted after the pandemic, utilizing Das Gupta decomposition analysis [20]. We broke down the changes in ADs burden into contributions from aging, population growth, and epidemiological changes during the periods post-pandemic (2019–2021) and pre-COVID-19 (2017–2019). This method allows for the evaluation of the independent contributions of each factor, providing insights into how demographic and epidemiological elements had evolved post-pandemic.

The fifth objective was to investigate the link between the COVID-19 incidence, vaccination rates, and the increased burden of ADs post-2019. Initially, we explored the correlation between COVID-19 incidence and changes in ADs without considering the impact of vaccination, utilizing data from 2020 since most vaccination campaigns were implemented after 2021. Given the heterogeneity in non-pharmacological

interventions for COVID-19—such as the use of masks, personal hygiene practices, and lockdown policies—as well as ethnic and geographic differences among various countries, we anticipated potential biases in country-level correlation analysis. To mitigate these, we analyzed data at the state level (51 states in the United States), district level (150 districts in England), and prefecture level (47 prefectures in Japan). A Spearman correlation analysis was employed, with the relative increases in ASIR/ASPR of ADs in 2020 as dependent variables and the ASIR of COVID-19 in 2020 as independent variables. Subsequently, we examined the relationship between COVID-19 vaccination rates and the increased burden of ADs at the state level in the USA, utilizing vaccination data up to December 31, 2021, within a 31-day window (15 days before and after December 31, 2021). A Spearman correlation analysis was applied, with the relative increase in ASIR/ASPR of ADs in 2021 as the dependent variable and the vaccination rate in 2021 as the independent variable.

All statistical analyses were conducted with R software, version 4.2.2.

## 3. Results

### 3.1. Impact of COVID-19 on global and regional burdens of ADs

We first analyzed the trends of ASR from 1990 to 2021 to determine whether the year 2019 was the joinpoint for increased burden (global and 5 SDI regions) for five ADs. (Figs. 1 and 2 & Table 1). The absolute and relative increases in ASR of burden after 2019 were presented in Fig. 2, Fig. S2 & Tables S1–3.

The absolute and relative increases in ASR of ADs burden after 2019 were analyzed across different 21 geographical regions and 204 countries/territories (Fig. 2 & Fig. S2 & Tables S4–6 & Figs. S5–9). Trends of ASR was also analyzed for these locations (Figs. 2 and 3 & Table 2 & Fig. S10 & Tables S8–13). The absolute differences of age-specific rates between 2021 and 2019 were presented in Fig. 4. The impact of age, population growth, and epidemiological changes on the incidence and prevalence of ADs prior to and during the COVID-19 pandemic across 5 SDI regions and 21 geographical regions were evaluated by decomposition analysis (Fig. 5). We also analyzed the association between COVID-19 incidence and increased disease burden of ADs in three countries with comprehensive data, namely the USA, England and Japan (Fig. 6A–S11 and S12). The association between the COVID-19 vaccination and increased burden of ADs in USA after 2019 was also examined (Fig. 6B).

### 3.2. Impact on disease burden of psoriasis

Joinpoint regression analysis pinpointed 2019 as the pivotal year for the disease burden of PsO (Figs. 1 and 2, Table 1). Specifically, the ASIR, ASPR, and ASDR all changed from a decreasing trend or plateau (with negative or zero APCs) before COVID-19 to a rising trend (positive APCs) after 2019 (Table 1). Compared to 2019, the growth in incident cases of PsO was 194.1 $\times$ $10^3$ in 2021. The ASIR rose from 61.2 (95 % UI 59.4 to 63.1) in 2019 to 62 (95 % UI 60.1 to 63.9) per 100,000 in 2021, with an absolute difference in ASIR of 0.78 per 100,000 (relative increase, 1.3 %) (Table S1). Compared to 2019, the global increase in prevalent cases of PsO reached 1651.3 $\times$ $10^3$ in 2021 (absolute difference in ASPR of 5 per 100,000, Table S2). PsO also showed a global increase of 131.4 $\times$ $10^3$ DALYs in 2021 compared to 2019 (increased ASDR of 0.33 DALYs per 100,000, Table S3).

The year 2019 was a joinpoint in all SDI regions, with increases in APCs of ASIR and ASPR, except for the high-middle SDI region. The high SDI region showed the largest increase in absolute differences in ASIR (1.94 per 100,000 in 2021), while the low-middle and middle SDI regions had the highest increases for ASPR (10.95 and 8.28 per 100,000 compared to 2019, respectively) and DALYs (0.85 and 0.62 per 100,000, respectively).

The burden of ASIR and ASPR on PsO showed an increase, except for African countries/territories. Notably, regions such as Western Europe,

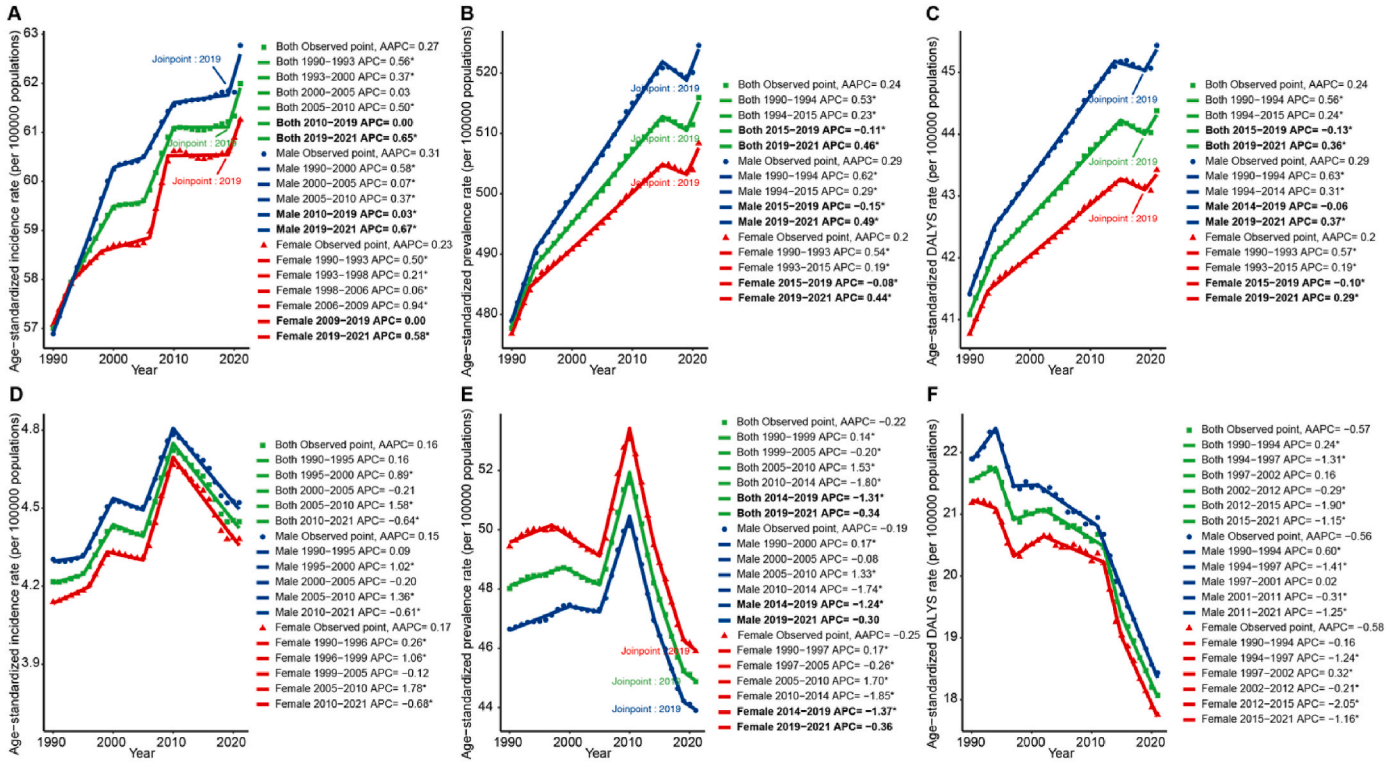


**Fig. 1.** Joinpoint regression analysis of global disease burden of psoriasis (A–C) and inflammatory bowel disease (D–F) from 1990 to 2021 by sex (both sexes in green, females in red, males in blue lines). Disease burden measures include age-standardized incidence rates (A & D), age-standardized prevalence rates (B & E), and age-standardized DALYs rates (C & F). APC = annual percentage change. AAPC = Average annual percentage change. *p < 0.05.

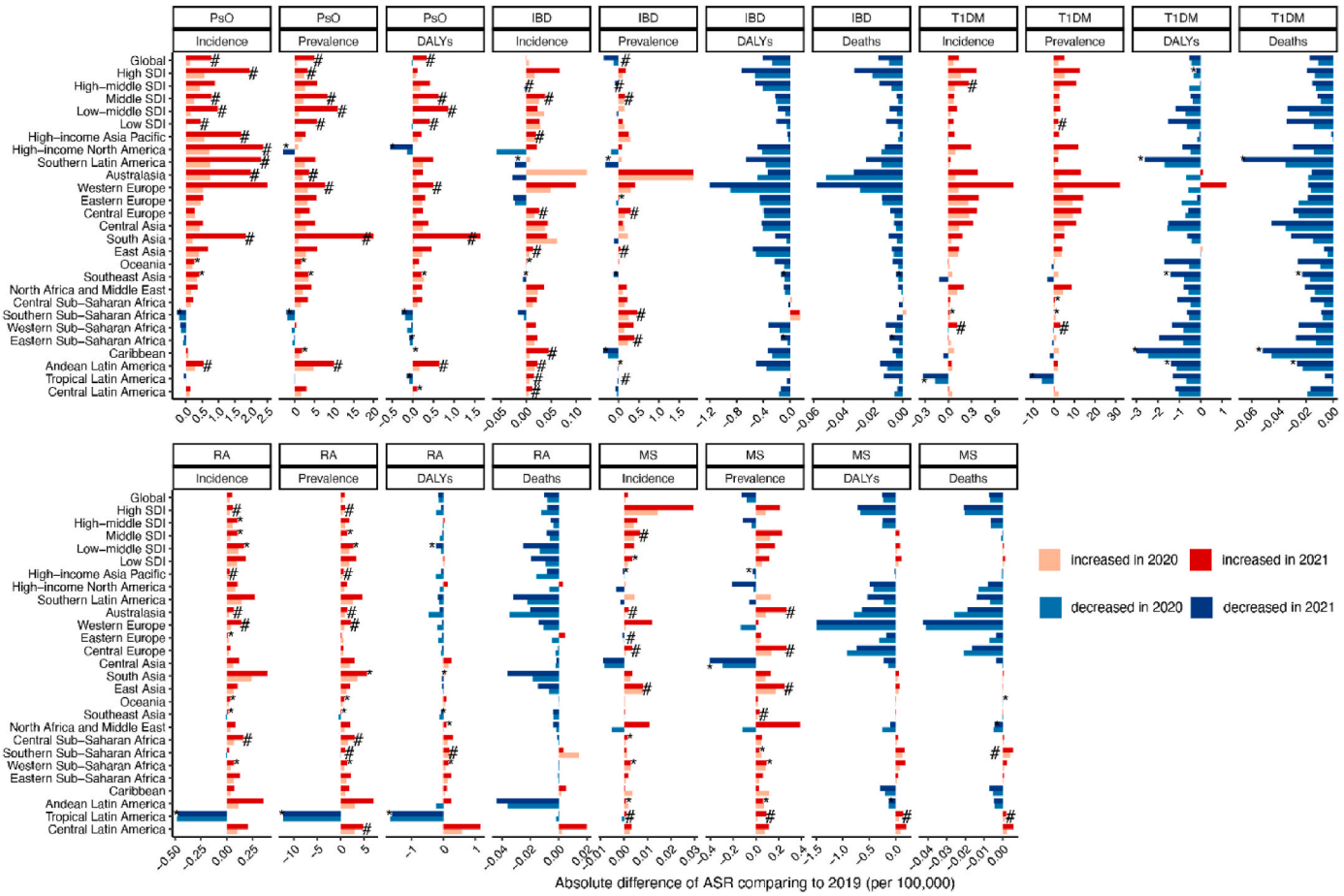


**Fig. 2.** The absolute difference in age-standardized rates (ASR) comparing 2021 to 2019 and 2020 to 2019 across global, five socio-demographic index (SDI) regions, and 21 geographical regions. Dark red and dark blue denote comparisons between 2021 and 2019, while light red and light blue represent comparisons between 2020 and 2019. The shades of blue, whether light or dark, indicate a decrease, whereas the shades of red, whether light or dark, signify an increase. # or * marked regions where 2019 was identified as a joinpoint for the trends of ASR. # indicates regions had increased annual percentage changes (APCs) of ASR post 2019 compared to the time segment before 2019, whereas * indicates regions had decreased APCs post 2019.

High-income North America, and Southern Latin America experienced a significant rise in incidence (increased ASIR from 2.3 to 2.5 per 100,000 when comparing 2021 to 2019, Fig. 2 & Table 2). High-income countries in Western Europe showed significantly increased ASIR or ASPR, with 2019 being identified as a joinpoint (Fig. 3). The most substantial increase in ASPR and ASDR was observed in South Asia in 2021, largely driven by data from India (increased ASPR, 24.6 per 100,000; increased ASDR, 2.0 per 100,000) (Fig. S5 & Table S9).

PsO also demonstrated increased incidence rates in 2021 among the 15 to 64 age group, with a peak in the 50 to 54 age group (marked at 3.05 per 100,000). The increased prevalence and DALY rates of PsO were highest in the 60–64 age groups (13.8 and 0.95 per 100,000 population, respectively). The increased burdens of PsO were more pronounced in males globally but such observation varied across different regions (Figure S3 & Figure S4 & Table S7 & Table S8).

Decomposition analysis showed the overall patterns of epidemiological changes in the burden of PsO had shifted in two years since 2019 compared to the period before 2019. From 2017 to 2019, global epidemiological changes in PsO contributed to a 0.2 % increase in incidence and a −0.18 % change in prevalence. These percentages rose to 1.33 % and 1 % for incidence and prevalence, respectively, during the period from 2019 to 2021. The increasing contribution of epidemiological changes in incidence and prevalence was also detected in regions, with 2019 as a joinpoint marking increased APCs of ASR post-2019 (Table S14).

### 3.3. Impact on disease burden of inflammatory bowel disease

The year 2019 also marked a turning point in the global ASPR for IBD, with increased APC after 2019 (Fig. 1 & Table 1). The global prevalent cases of IBD increased by $96.6 \times 10^3$ cases in 2021 compared to 2019 (absolute difference of ASPR, −0.37 per 100,000, Table S2). Compared to 2019, high and middle SDI regions had the highest increased ASIR (0.067 and 0.037 per 100,000, respectively) and increased ASPR (0.18 and 0.16 per 100,000) in 2021 (Table 1 & Fig. 2).

Significant increases in APCs of ASPR with 2019 as a joinpoint were observed in regions of Southern and Eastern Sub-Saharan Africa, Central Europe, and East Asia. Australia reported the highest increased ASPR in 2021 among all countries/territories (2.26 per 100,000) (Fig. S6 & Table S10). The highest absolute increases in incidence rate for IBD were observed in the 40 to 44 age groups, with rates of 0.13 per 100,000 populations (Fig. 4).

Decomposition analysis also showed shifts in the overall patterns of epidemiological changes two years after 2019. Global epidemiological changes attributed −1.9 % to incidence and −2.56 % to prevalence from 2017 to 2019. These percentages shifted to −0.01 % and −0.86 % for incidence and prevalence, respectively, between 2019 and 2021. The increasing contribution of epidemiological changes in incidence and prevalence was also detected in geographical regions as mentioned above, with 2019 as a joinpoint marking the increase in APCs of ASR (Table S15).

**Table 1**
Results for joinpoint regression analysis of age-standardized rates (ASR) for five autoimmune diseases from 1990 to 2021 for global and five SDI regions. Regions where 2019 was identified as a joinpoint, demonstrating an increased annual percentage change (APC) after 2019 compared to the preceding time segment, are presented.

| measure | location | time segment before 2019 | APC 95 % CI (before 2019) | APC 95 % CI (2019–2021) |
|---|---|---|---|---|
| **PsO** | | | | |
| Incidence | Global | 2010 to 2019 | 0 (−0.01 to 0.02) | 0.65 (0.51–0.8) |
| Incidence | High SDI | 2015 to 2019 | 0.21 (−0.03 to 0.44) | 1.05 (0.57–1.54) |
| Incidence | Low SDI | 2016 to 2019 | 0 (−0.19 to 0.19) | 0.58 (0.38–0.77) |
| Incidence | Low-middle SDI | 2016 to 2019 | −0.13 (−0.31 to 0.05) | 0.96 (0.77–1.15) |
| Incidence | Middle SDI | 2015 to 2019 | 0.22 (0.16–0.27) | 0.62 (0.51–0.73) |
| Prevalence | Global | 2015 to 2019 | −0.11 (−0.19 to −0.03) | 0.46 (0.3–0.63) |
| Prevalence | High SDI | 2015 to 2019 | 0.03 (−0.03 to 0.08) | 0.2 (0.08–0.31) |
| Prevalence | Low SDI | 2016 to 2019 | −0.1 (−0.41 to 0.22) | 1.01 (0.7–1.32) |
| Prevalence | Low-middle SDI | 2016 to 2019 | −0.4 (−0.68 to −0.12) | 1.48 (1.19–1.76) |
| Prevalence | Middle SDI | 2015 to 2019 | 0.24 (0.2–0.28) | 0.81 (0.73–0.89) |
| DALYs | Global | 2015 to 2019 | −0.13 (−0.22 to −0.04) | 0.36 (0.18–0.54) |
| DALYs | Low SDI | 2016 to 2019 | −0.13 (−0.41 to 0.15) | 0.89 (0.61–1.18) |
| DALYs | Low-middle SDI | 2016 to 2019 | −0.34 (−0.64 to −0.04) | 1.32 (1.02–1.63) |
| DALYs | Middle SDI | 2015 to 2019 | 0.23 (0.16–0.31) | 0.69 (0.54–0.84) |
| **RA** | | | | |
| Incidence | High SDI | 2011 to 2019 | −0.37 (−0.42 to −0.33) | 0.16 (−0.18 to 0.5) |
| Prevalence | High SDI | 2011 to 2019 | −0.33 (−0.38 to −0.29) | 0.18 (−0.16 to 0.53) |
| **MS** | | | | |
| Incidence | Middle SDI | 2014 to 2019 | 0.46 (0.42–0.51) | 0.72 (0.58–0.87) |
| **IBD** | | | | |
| Incidence | High-middle SDI | 2010 to 2019 | −1.25 (−1.36 to −1.15) | −0.29 (−1.34 to 0.78) |
| Incidence | Middle SDI | 2015 to 2019 | −1.76 (−2.75 to −0.77) | 1.02 (−0.97 to 3.04) |
| Prevalence | Global | 2014 to 2019 | −1.31 (−1.45 to −1.17) | −0.34 (−0.78 to 0.11) |
| Prevalence | High-middle SDI | 2010 to 2019 | −1.64 (−1.73 to −1.55) | −0.05 (−0.96 to 0.85) |
| Prevalence | Middle SDI | 2015 to 2019 | −1.85 (−2.96 to −0.72) | 0.62 (−1.66 to 2.95) |
| **T1DM** | | | | |
| Incidence | High-middle SDI | 2009 to 2019 | 1.37 (1.34–1.4) | 1.96 (1.57–2.35) |
| Prevalence | Low SDI | 2015 to 2019 | 0.32 (0.24–0.41) | 0.55 (0.37–0.73) |

Notes: PsO, psoriasis; IBD, inflammatory bowel disease; T1DM, type 1 diabetes; RA, rheumatoid arthritis; MS, multiple sclerosis; CI, confidence interval.

### 3.4. Impact on disease burden of type 1 diabetes mellitus, rheumatoid arthritis, and multiple sclerosis

Unlike PsO and IBD, the year 2019 did not appear to be a significant global turning point for the incidence, prevalence, and DALYs for T1DM, RA, and MS (Figure S1 & Fig. 2).

However, these three ADs showed geographical-specific changes. For T1DM, the year 2019 did not mark a change in trends of ASIR and ASPR, except in Western Sub-Saharan Africa. The most significant absolute increases in ASIR, ASPR, and ASDR for T1DM were observed in Western Europe (Fig. S7 & Table S11). For RA, there were significant increases in APCs of ASPR, with 2019 as the joinpoint, in Central and Southern Sub-Saharan Africa, Western Europe, Australasia, and High-income Asia Pacific (increased ASPR ranging from 2.9 to 0.67 per 100,000). Norway, the United Kingdom, and Colombia also identified 2019 as a joinpoint (increased ASPR in 2021 ranging from 8.5 to 6.6 per 100,000, Fig. S8 & Table S12). For MS, Sweden experienced an absolute increase in ASIR of 0.2 and ASPR of 6.6 per 100,000. It is noteworthy that China, representing East Asia, showed the highest increased relative percentage of ASIR and ASPR in 2021 compared to 2019, at 5.3 % and 13.2 %, respectively (Figure S9 & Figure S10 & Table S13).

The highest absolute increases in incidence rate for T1DM, RA, and MS were observed in the 20 to 24, 75 to 79, and 40 to 44 age groups, with rates of 0.25, 0.74, and 0.027 per 100,000 populations, respectively.

Decomposition analysis showed the overall patterns of epidemiological changes in the burden of these three ADs had remained largely consistent post-2019, although geographical effects were still observed (Table S16, S17 and S18). Notably, for MS, the epidemiological change in prevalence in East Asia was 3.35 % from 2017 to 2019, with the percentage increasing significantly to 12.8 % from 2019 to 2021.

### 3.5. Associations between COVID-19 infection and increased burdens of ADs

We initially examined the relationship between COVID-19 incidence and changes in ADs using data up to the end of 2020. Among 51 states in USA, ASIR of COVID-19 in 2020 was found to be significantly positively correlated with the relative increase in ASIR and ASPR of PsO (Spearman $R = 0.35$ and $p = 0.01$ for both measures, Fig. 6A). Similar positive correlations for ASIR and ASPR of PsO were validated in 150 districts in England (R: 0.24 and 0.2, respectively; $p < 0.001$ and $p = 0.017$, respectively; Fig. S11) and 47 prefectures in Japan (R: 0.36, and 0.36, respectively; $p = 0.014$ and 0.012, respectively; Fig. S12). We further evaluated the relationship between COVID-19 vaccination rates as of December 31, 2021, and the increased burden of ADs in 2021 across 49 states with available vaccination data (Table S19). In the USA, state-level vaccination rates in 2021 were significantly negatively correlated with the relative increase in ASIR of PsO and RA (R: 0.27 and −0.54, respectively; all $p < 0.001$, Fig. 6B), as well as the increase in ASPR of PsO, RA, and MS (R: 0.45, −0.49, and −0.41, respectively; all $p < 0.01$, Fig. 6B).

## 4. Discussions

### 4.1. Principal findings

The results revealed that 2019 was a joinpoint indicating global rises in incidence, prevalence, and DALYs of PsO. For PsO, higher increased incidence rates in 2021 were found in high SDI regions, particularly in the 50 to 54 age group and among males. Increased prevalence and DALYs burdens of PsO were predominantly observed in low-middle and middle SDI regions and among the 60–64 age group. Furthermore, 2019 also served as a turning point, highlighting a rise in ASIR and ASPR post-2019 across several geographical regions for PsO (high-income North America, Southern Latin America, and South Asia), IBD (Southern and Eastern Sub-Saharan Africa, Central Europe, and East Asia), T1DM (Western Sub-Saharan Africa), RA (Central and Southern Sub-Saharan Africa, Western Europe, Australasia, and High-income Asia Pacific), and MS (East Asia, Central Europe). Many countries experienced a significant increase in ASIR and ASPR after 2019, as identified by joinpoint regression analysis. Decomposition analysis demonstrated that the

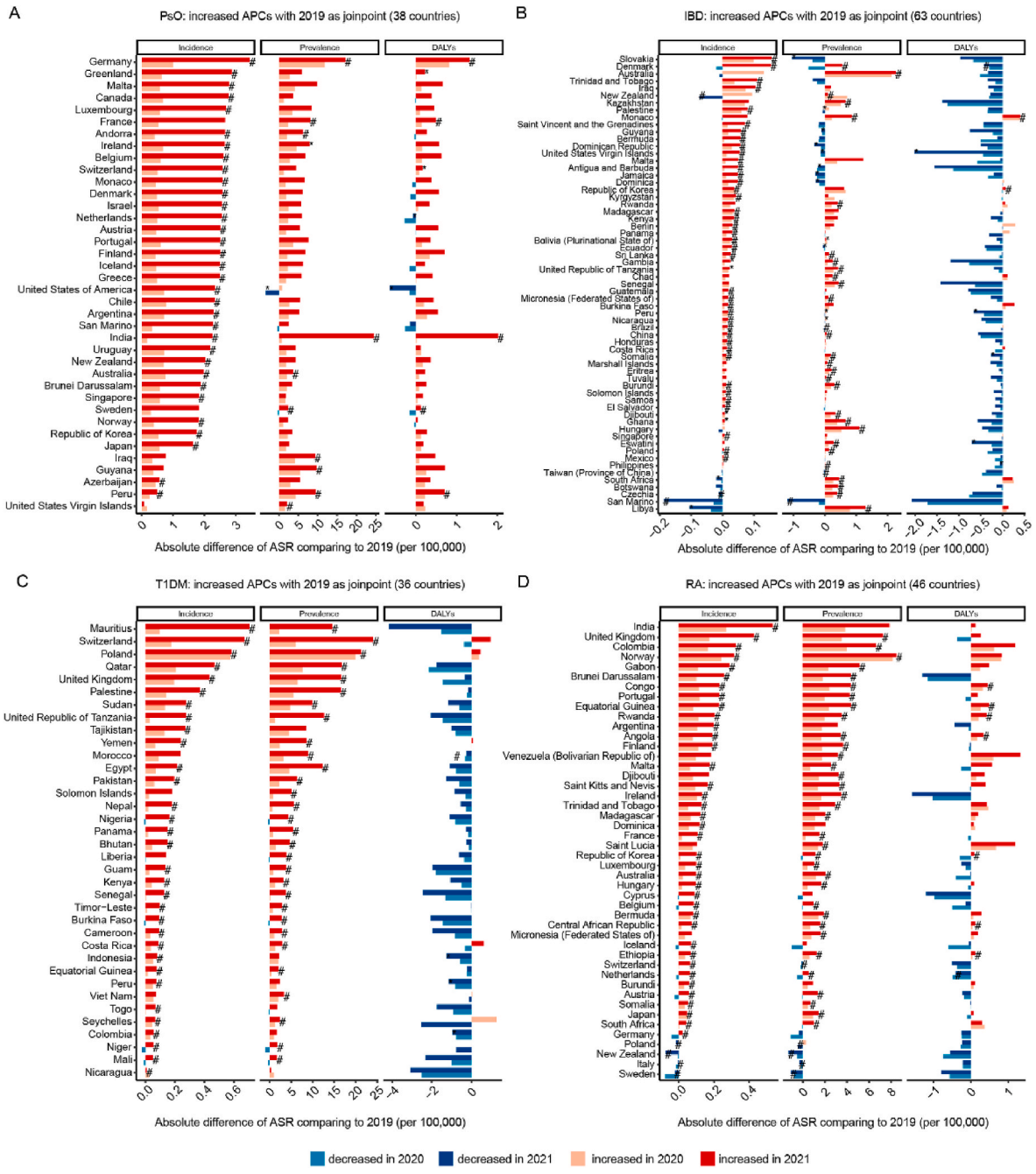


**Fig. 3.** Countries/territories with 2019 as joinpoints in trends of age-standardized rates (ASR) of incidence or prevalence for psoriasis (A), inflammatory bowel disease (B), inflammatory bowel disease (C), and rheumatoid arthritis (D). Countries/territories had increased annual percentage changes (APCs) in ASR of incidence or prevalence post 2019 compared to the time segment before 2019. Dark red and dark blue denote comparisons between 2021 and 2019, while light red and light blue represent comparisons between 2020 and 2019. The shades of blue, whether light or dark, indicate a decrease, whereas the shades of red, whether light or dark, signify an increase. # or * marked locations where 2019 was identified as a joinpoint for the trends of ASR. # indicates locations had increased APCs of ASR post 2019 compared to the time segment before 2019, whereas * indicates locations had decreased APCs change post 2019.

increased burden for these regions was driven by epidemiological changes rather than demographic changes. State-level data from the USA indicated a positive correlation between COVID-19 incidence and the increased burden of PsO, while vaccination may exhibit a protective effect.

### 4.2. *Significantly increased burden of PsO two years after the pandemic*

The year 2019 witnessed significant shifts in the global burden of PsO two years after the onset of the COVID-19 pandemic. The observed higher ASIR in males and the most affected age group of 50–54 years aligns with the typical gender and age predilection for PsO [21,22]. Countries from high-SDI regions, Western Europe, High-income North America, and Southern Latin America experienced the most significant increase in incidence for PsO, consistent with known disease susceptibility patterns [23]. Of note, India, representing South Asia, has experienced a significant increase in the prevalence and DALYs of PsO. This surge can be attributed to the underdeveloped healthcare infrastructure in various regions with lower SDI, which was significantly overwhelmed during the pandemic [24]. The global rise in DALYs of PsO has profound

**Table 2**
Results for joinpoint regression analysis of age-standardized rates (ASR) for five autoimmune diseases from 1990 to 2021 for 21 geographical regions. Regions where 2019 was identified as a joinpoint, demonstrating an increased annual percentage change (APC) after 2019 compared to the preceding time segment, are presented.

| measure | location | time segment before 2019 | APC 95 % CI (before 2019) | APC 95 % CI (2019–2021) |
|---|---|---|---|---|
| **PsO** | | | | |
| Incidence | Andean Latin America | 2015 to 2019 | −0.04 (−0.14 to 0.07) | 0.26 (0.03–0.5) |
| Incidence | Australasia | 2015 to 2019 | −0.69 (−0.86 to −0.52) | 1.37 (1.01–1.74) |
| Incidence | High-income Asia Pacific | 2015 to 2019 | −0.04 (−0.35 to 0.27) | 1.52 (0.88–2.17) |
| Incidence | High-income North America | 2015 to 2019 | 0.33 (0.12–0.54) | 1.14 (0.71–1.57) |
| Incidence | South Asia | 2016 to 2019 | −0.55 (−0.79 to −0.31) | 1.89 (1.64–2.14) |
| Incidence | Southern Latin America | 2015 to 2019 | 0.38 (0.12–0.63) | 1.48 (0.95–2.01) |
| Prevalence | Andean Latin America | 2015 to 2019 | −0.16 (−0.26 to −0.06) | 0.53 (0.3–0.76) |
| Prevalence | Australasia | 2015 to 2019 | −1.22 (−1.36 to −1.08) | 0.44 (0.13–0.74) |
| Prevalence | South Asia | 2016 to 2019 | −1.29 (−1.65 to −0.92) | 2.9 (2.52–3.28) |
| Prevalence | Western Europe | 2015 to 2019 | −0.2 (−0.25 to −0.14) | 0.33 (0.21–0.44) |
| DALYs | Andean Latin America | 2015 to 2019 | −0.19 (−0.32 to −0.06) | 0.4 (0.14–0.66) |
| DALYs | South Asia | 2016 to 2019 | −1.24 (−1.59 to −0.88) | 2.74 (2.38–3.1) |
| DALYs | Western Europe | 2015 to 2019 | −0.2 (−0.27 to −0.14) | 0.25 (0.11–0.38) |
| **RA** | | | | |
| Incidence | Australasia | 2011 to 2019 | −0.96 (−0.98 to −0.93) | 0.22 (0.02–0.41) |
| Incidence | Central Sub-Saharan Africa | 2010 to 2019 | 0.99 (0.96–1.01) | 1.2 (0.99–1.41) |
| Incidence | High-income Asia Pacific | 2014 to 2019 | −1.42 (−1.51 to −1.33) | 0.2 (−0.08 to 0.49) |
| Incidence | Western Europe | 2012 to 2019 | −0.21 (−0.23 to −0.18) | 0.42 (0.26–0.57) |
| Prevalence | Australasia | 2012 to 2019 | −0.9 (−0.93 to −0.88) | 0.34 (0.2–0.49) |
| Prevalence | Central Latin America | 2010 to 2019 | 0 (−0.01 to 0.02) | 0.74 (0.58–0.89) |
| Prevalence | Central Sub-Saharan Africa | 2011 to 2019 | 1.02 (1–1.05) | 1.39 (1.19–1.58) |
| Prevalence | High-income Asia Pacific | 2014 to 2019 | −1.46 (−1.57 to −1.35) | 0.28 (−0.08 to 0.64) |
| Prevalence | Southern Sub-Saharan Africa | 2011 to 2019 | −0.5 (−0.51 to −0.49) | 0.23 (0.14–0.32) |
| Prevalence | Western Europe | 2011 to 2019 | −0.12 (−0.14 to −0.1) | 0.4 (0.23–0.57) |
| DALYs | Southern Sub-Saharan Africa | 2012 to 2019 | −1.13 (−1.42 to −0.85) | 0.24 (−1.49 to 2) |
| **MS** | | | | |
| Incidence | Australasia | 2015 to 2019 | −2 (−2.32 to −1.68) | 0.08 (−0.63 to 0.8) |
| Incidence | Central Europe | 2011 to 2019 | −0.47 (−0.49 to −0.46) | 0.16 (0.06–0.26) |
| Incidence | East Asia | 2014 to 2019 | −0.25 (−0.4 to −0.1) | 2.68 (2.17–3.19) |
| Incidence | Eastern Europe | 2008 to 2019 | −0.58 (−0.59 to −0.57) | 0.06 (−0.06 to 0.18) |
| Incidence | Tropical Latin America | 2015 to 2019 | −1.22 (−1.51 to −0.92) | 0.1 (−0.5 to 0.71) |
| Prevalence | Australasia | 2015 to 2019 | −2.08 (−2.69 to −1.47) | 0.22 (−1.23 to 1.68) |
| Prevalence | Central Europe | 2011 to 2019 | −0.18 (−0.21 to −0.16) | 0.35 (0.16–0.54) |
| Prevalence | East Asia | 2014 to 2019 | 1.4 (1.3–1.5) | 6.23 (5.91–6.55) |
| Prevalence | Southeast Asia | 2011 to 2019 | 0.59 (0.58–0.6) | 0.68 (0.62–0.74) |
| Prevalence | Tropical Latin America | 2014 to 2019 | −0.93 (−1.15 to −0.71) | −0.01 (−0.72 to 0.7) |
| DALYs | Tropical Latin America | 2012 to 2019 | −1.64 (−1.9 to −1.38) | 0.39 (−1.26 to 2.06) |
| Deaths | Southern Sub-Saharan Africa | 2013 to 2019 | −0.23 (−0.74 to 0.29) | 2.76 (−0.45 to 6.07) |
| Deaths | Tropical Latin America | 2011 to 2019 | −3.25 (−3.64 to −2.86) | 1.04 (−2.87 to 5.1) |
| **IBD** | | | | |
| Incidence | Andean Latin America | 2015 to 2019 | −0.87 (−0.98 to −0.76) | 0.82 (0.58–1.06) |
| Incidence | Caribbean | 2010 to 2019 | 0.2 (0.16–0.23) | 0.77 (0.47–1.08) |
| Incidence | Central Europe | 2015 to 2019 | −2.42 (−2.75 to −2.09) | 0.41 (−0.33 to 1.16) |
| Incidence | Central Latin America | 2015 to 2019 | −1.04 (−1.83 to −0.24) | 1.17 (−0.47 to 2.84) |
| Incidence | East Asia | 2015 to 2019 | −6.47 (−8.36 to −4.54) | 0.91 (−2.99 to 4.97) |
| Incidence | High-income Asia Pacific | 2012 to 2019 | −2.74 (−2.97 to −2.51) | 0.56 (−1.14 to 2.29) |
| Incidence | Tropical Latin America | 2015 to 2019 | −6.34 (−7.7 to −4.97) | 0.8 (−2.05 to 3.74) |
| Prevalence | Central Europe | 2015 to 2019 | −2.79 (−3.34 to −2.24) | 0.45 (−0.74 to 1.65) |
| Prevalence | East Asia | 2015 to 2019 | −8.32 (−9.74 to −6.88) | 0.8 (−2.31 to 3.99) |
| Prevalence | Eastern Sub-Saharan Africa | 2010 to 2019 | 0.83 (0.8–0.87) | 1.49 (1.18–1.8) |
| Prevalence | Southern Sub-Saharan Africa | 2015 to 2019 | 0.69 (0.58–0.81) | 1.36 (1.14–1.59) |
| Prevalence | Tropical Latin America | 2015 to 2019 | −6.01 (−7.33 to −4.66) | 0.51 (−2.23 to 3.32) |
| **T1DM** | | | | |
| Incidence | Western Sub-Saharan Africa | 2002 to 2019 | 0.2 (0.18–0.22) | 1.07 (0.55–1.59) |
| Prevalence | Western Sub-Saharan Africa | 2002 to 2019 | 0.23 (0.2–0.25) | 0.97 (0.3–1.65) |

Notes: PsO, psoriasis; IBD, inflammatory bowel disease; T1DM, type 1 diabetes; RA, rheumatoid arthritis; MS, multiple sclerosis; CI, confidence interval.

implications, affecting patient morbidity and healthcare service utilization. Beyond skin lesions, around one-third of PsO patients develop psoriatic arthritis, which can progress into joint deformities, impairing patients' functional status and quality of life [25,26]. PsO also increases the risks of cardiometabolic comorbidities and adverse cardiovascular outcomes [25,27,28], in addition to leading to toxicities and escalating treatment costs [29,30].

### *4.3. Changes in burden of IBD, T1DM, RA and MS post the COIVD-19 pandemic*

Although the increases in burdens of IBD, T1DM, RA, and MS were not as pronounced as that of PsO, our study revealed sex-, age-, region-, and country-specific challenges. The pandemic appeared to have the least impact on ASIR and ASPR of T1DM, as 2019 did not emerge as a joinpoint in most geographical regions. These findings are consistent with a study from Denmark, which reported an increased incidence of T1DM following the pandemic but found no correlation with SARS-CoV-2 infection [15]. Surprisingly, rising trends of ADs were observed in some regions with generally lower prevalence, such as an increased T1DM burden in Western Sub-Saharan Africa and an increased IBD burden in Southern and Eastern Sub-Saharan Africa. This probably correlated with extremely low vaccination rates in Africa by the end of 2021 due to vaccine nationalism and vaccine diplomacy [31]. These trends present challenges for Sub-Saharan Africa with insufficient

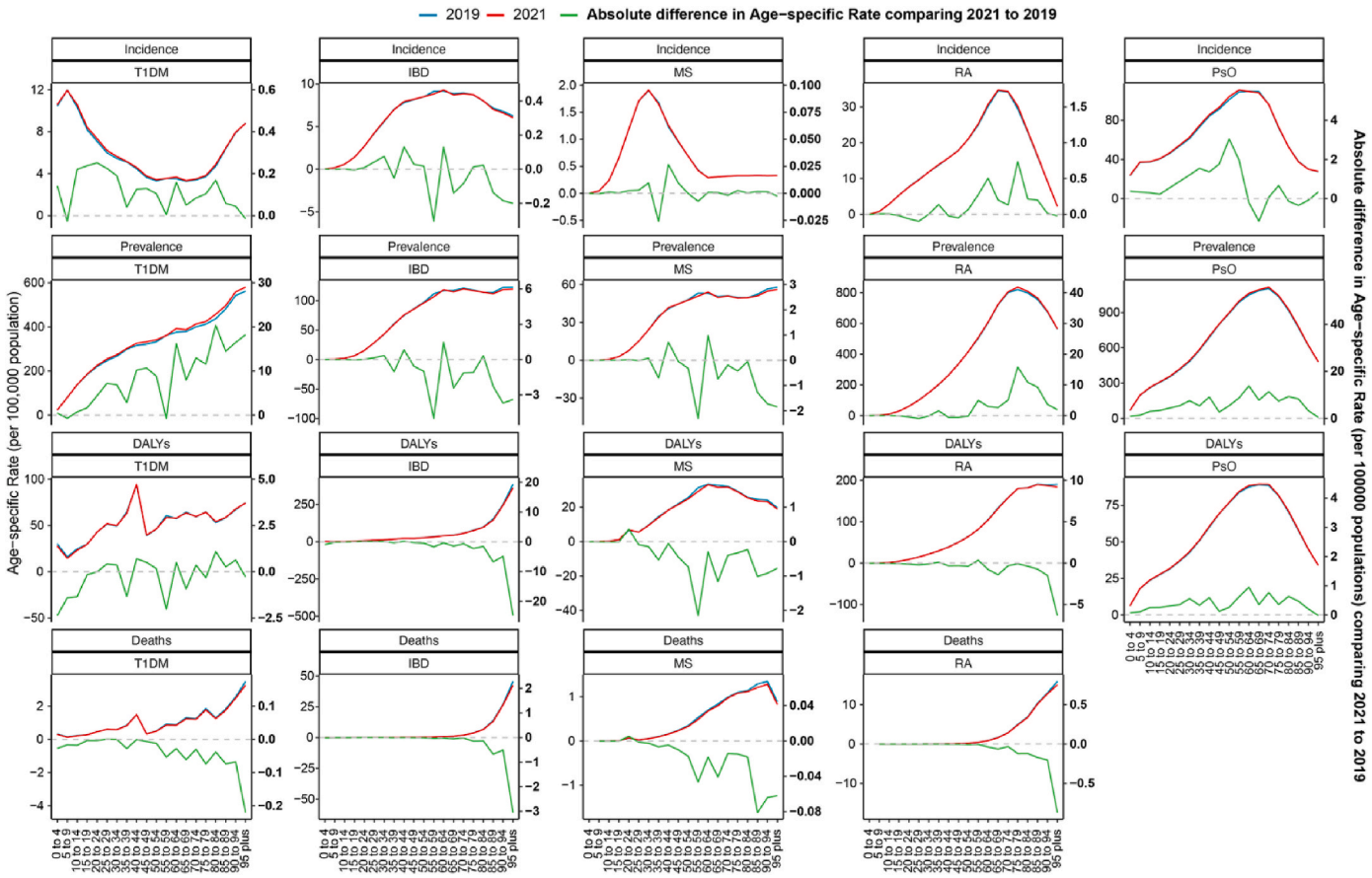


**Fig. 4.** Change in disease burden across different age groups comparing 2021 to 2019. Global age-specific rates for 2021 and 2019 are depicted in red and blue, respectively, with the y-axis on the left. The absolute differences in age-specific rates comparing 2021 to 2019 are shown in green lines with the y-axis on the right. The x-axis denotes the age groups from 0 to 95 plus years old by five-year intervals.

diagnostic capacity and a higher risk of complications and mortality associated with these autoimmune diseases [32,33]. For MS, significant epidemiological shifts were detected in East Asia, represented by China. Despite China's overall low infection rate two years post-pandemic, the increased burden might be related to the high severity rates caused by the first wave of infections and treatment disruptions [12]. While there were no substantial worldwide increases in DALYs and mortality burden for these four autoimmune diseases following the COVID-19 pandemic, regions and countries experiencing an increased burden should formulate effective strategies to address these issues, considering their healthcare infrastructure and resources.

### *4.4. Associations between COVID-19 incidence, vaccination uptake rates, and increased burdens of ADs*

According to decomposition analysis, the increase in disease burden was largely driven by epidemiological changes. It is reasonable to correlate these epidemiological increases with the COVID-19 pandemic, given the massive infection rates and evidence suggesting a heightened risk of developing these ADs following COVID-19 infection [4,7,8,34–36]. A positive correlation between COVID-19 incidence and the increased burden of PsO was observed in the first year after the pandemic in the USA, UK, and Japan. The results further underscored the protective effect of vaccination in PsO, aligning with the latest findings [35], despite earlier concerns regarding reports of PsO following COVID-19 vaccination [37,38]. A protective effect of vaccination on increased burden of MS and RA was identified, reinforcing the consensus regarding the role of COVID-19 vaccination in managing MS [39,40] and RA [41].

### *4.5. Differential changes in disease burden for different ADs after COVID-19 – putative mechanisms*

The exact mechanism of how SARS-CoV-2 infection may enhance the risk of ADs remains unclear. Currently available evidence has implicated the role for molecular mimicry, bystander activation, breaching of tolerogenic pathways, and abnormal nucleic acid sensing [42–45]. We postulated that SARS-CoV-2 may be more potent in triggering distinct immune-reactive cells and pathways. In this study, SARS-CoV-2 infection was associated with a significant shift in burden of PsO and IBD, both of which showed strong links with $CD4^+$ (especially Th17 cells) and $CD8^+$ type 1 T cells and related cytokine/inflammatory pathways (TNF-α, IFN-γ, IL-2, IL-17/23), with more prominent activation of cell-mediated rather than humoral immune response [46–49]. As for RA, T1DM and MS, the pathogenesis may be more complex and involves both T and B cell immunity as it is well recognized that these autoimmune conditions are frequently associated with pathogenic autoantibodies (e.g. anti-citrullinated protein antibodies (ACPAs), anti-islet autoantibodies (IAA), anti-glutamic acid decarboxylase (anti-GADA), anti-glutamic acid decarboxylase (anti-GAD), anti-myelin oligodendrocyte glycoprotein (anti-MOG), anti-myelin basic protein (anti-MBP) [50–53].

### *4.6. Strengths and limitations of this study*

Our study found the COVID-19 pandemic significantly influenced the epidemiological trends of ADs both globally and regionally. Several limitations should be acknowledged in this study. Firstly, the findings are largely descriptive, and the causal relationship between COVID-19

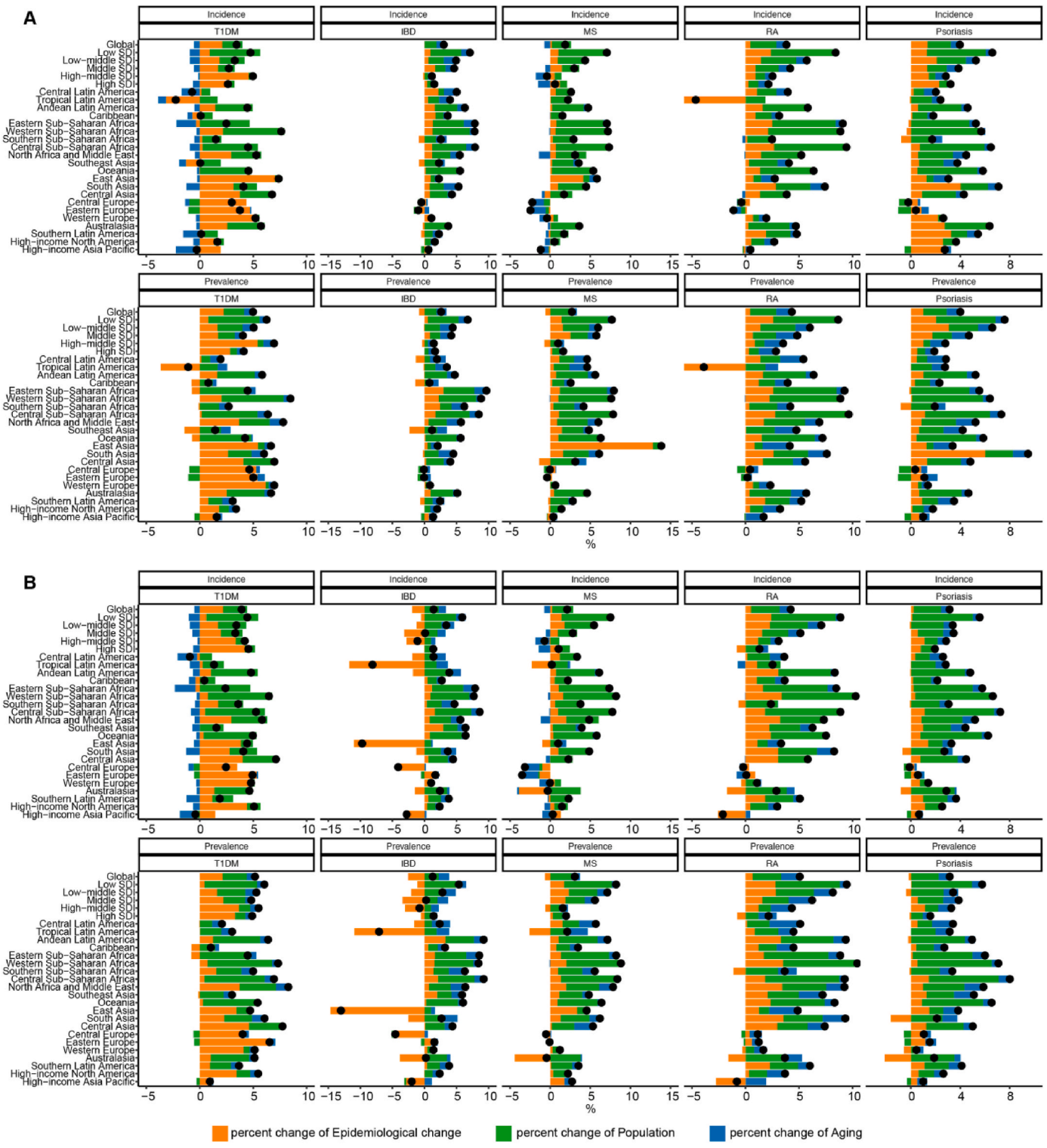


**Fig. 5.** Population-level determinant changes in aging, population growth, and epidemiological changes globally during the periods post-pandemic (A, 2019 to 2021) and pre-COVID-19 (B, 2017 to 2019). Black dots represent the total change contributed by all three components. A positive value for each component indicates a corresponding positive contribution, and a negative value indicates a corresponding negative contribution. The x-axis scale remains consistent within the same disease. PsO, psoriasis; IBD, inflammatory bowel disease; T1DM, type 1 diabetes; RA, rheumatoid arthritis; MS, multiple sclerosis.

infection, vaccination, and the burden of ADs has yet to be established. Secondly, significant disparities exist in race, healthcare systems, severity of COVID-19 infection, vaccination policies, non-pharmacological interventions, and environmental factors across countries. These disparities limit our ability to perform a correlation analysis at the county level. Additionally, due to data limitations, it is not feasible to validate the correlation results across other countries. Thirdly, with just two years of post-pandemic data available, it remains challenging to fully understand the epidemiological changes in ADs following COVID-19. Lastly, disruptions in healthcare services could lead to underdiagnosis of ADs and inaccuracies in data collection.

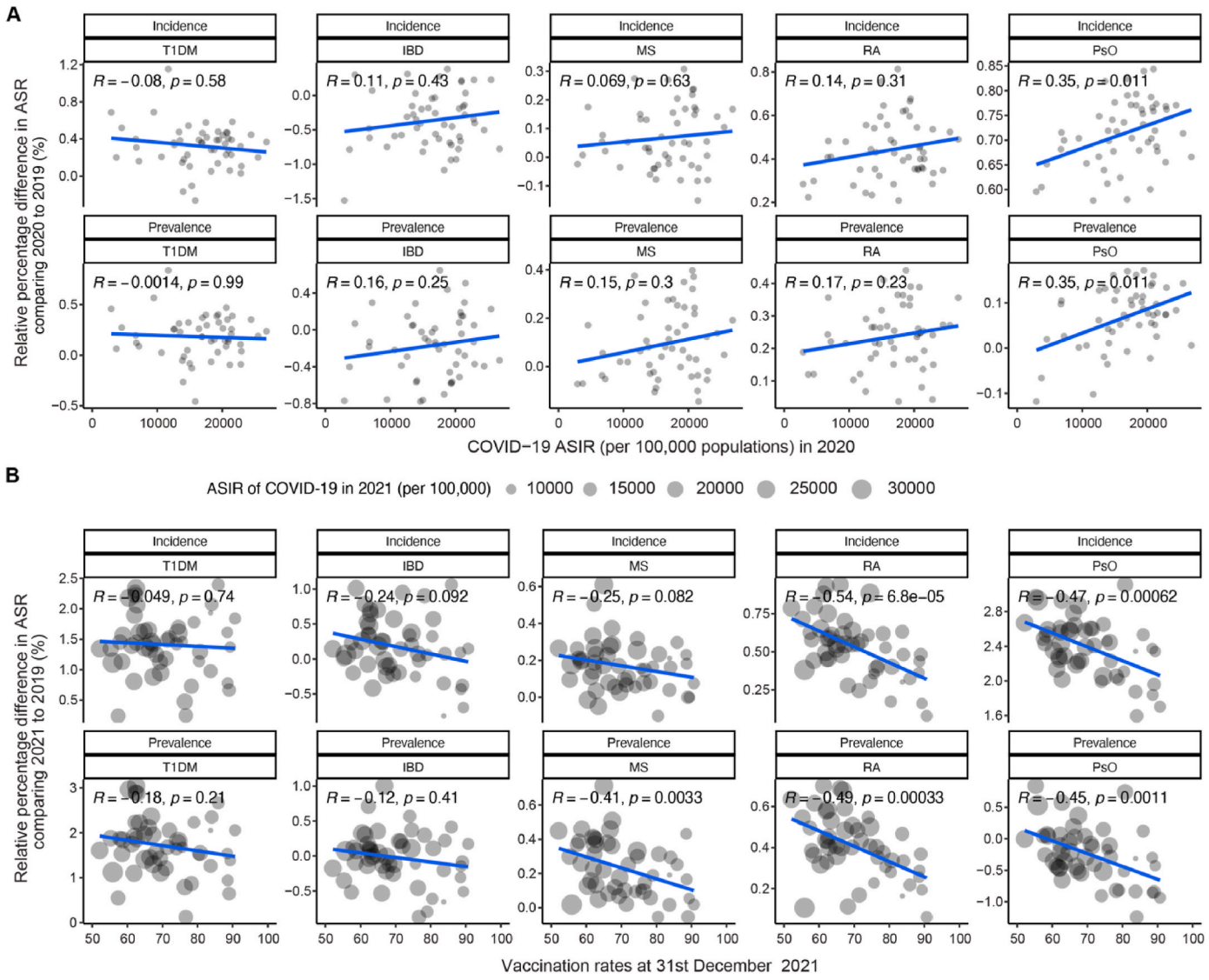


**Fig. 6.** (A) Dot plots with fitted linear regressions illustrate correlations between the COVID-19 ASIR (age-standardized incidence rates) in 2020 and the relative increases in ASR (age-standardized rates) of incidence and prevalence in 2020 compared to 2019 at the state level (51 states in the USA). (B) Dot plots show correlations between the vaccination rates on December 31, 2021, and the relative increased ASR of incidence and prevalence in 2021 compared to 2019 at state levels (49 states in the USA). Each bubble represents a country/territory, with the size of the bubble depicting the ASIR of COVID-19 (per 100,000) in 2021. Vaccination data on December 31, 2021, were obtained. Missing values were filled by data from a 31-day window (15 days before and after December 31, 2021). The results from the Spearman correlation analysis (R = correlation coefficient alongside its p-value) are presented in the figure. PsO, psoriasis; IBD, inflammatory bowel disease; T1DM, type 1 diabetes; RA, rheumatoid arthritis; MS, multiple sclerosis.

## 5. Conclusions

The year 2019 marked a pivotal point for increased global burden of PsO and regional burdens of other ADs. These observations have important implications for healthcare planning and resource allocation in the post-COVID-19 era.

## CRediT authorship contribution statement

**Danting Zhang:** Data curation. **Wanyu Hua:** Data curation. **Fangfang Sun:** Data curation. **Chao Wen:** Data curation. **Lai Yee Cheong:** Formal analysis. **Ruiyan Xie:** Data curation, Formal analysis. **Koon Ho Chan:** Resources. **Shirley C.W. Chan:** Resources. **Xue Li:** Formal analysis. **Shuang Ye:** Writing – original draft, Writing – review & editing. **Desmond Y.H. Yap:** Conceptualization, Supervision, Writing – review & editing.

## Ethical approval

Not required.

## Data sharing

Data used in the analyses can be obtained from the Global Health Data Exchange Global Burden of Disease Results Tool (https://vizhub.healthdata.org/gbd-results/) and Our World in Data (https://ourworldindata.org/covid-vaccinations).

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtauto.2025.100289.

## Data availability

Data will be made available on request.

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