receiving biologic DMARDs is well known, and patients have probably been informed of this risk at the time of treatment initiation (6,7).

Reduced physical activity resulting from home confinement could be another explanation for worsening symptoms. In SpA patients, exercise can reduce disease activity and, consequently, is recommended for optimal treatment (8).

In this patient population, COVID-19 occurrence was associated with SpA treatment modification. We did not find a link between NSAID or biologic treatment and COVID-19. When considering both the confirmed and the clinically suspected cases of COVID-19, we found 31 cases (13 clinically suspicious and 18 self-reported as being confirmed), which is more substantial than the 8 cases in a cohort of 320 patients with chronic arthritis (4 confirmed and 4 highly suggestive) reported by Monti et al (9). However, it is impossible to compare prevalence as the population, methodology, and period are different (9). It is important to emphasize that a majority of our patients were treated with NSAIDs. Our results are interesting because they provide data from a real-life setting.

Our findings should be interpreted within the limitations of the study. The most important limitation is that our results are based on self-reported data. For patients who reported having confirmed COVID-19, we could not verify that this was in fact confirmed via a positive test result. However, this is the first study providing information on therapy compliance during home confinement and reporting the frequency of COVID-19 in SpA patients. The size of our cohort reinforces the importance of our results.

Thus, our survey results show that in SPA patients, home confinement linked to the COVID-19 pandemic is associated with worsening of the disease and reduction or suspension of medication intake, in particular NSAIDs. These findings have considerable clinical implications, given that home confinement is likely to recur in the future. Patients need to be educated about the current evidence regarding NSAID treatment and ways to stay physically active at home.

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Morbidity and mortality from COVID-19 are not increased among children or patients with autoimmune rheumatic disease—possible immunologic rationale: comment on the article by Henderson et al

To the Editor:

We read with great interest the article by Henderson et al (1) on the therapeutic rationale for using glucocorticoids to treat the hyperinflammation and cytokine storm phases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. We would like to expand on their analysis and discuss the data reported to date on the likelihood of serious outcomes of infection in children and patients with autoimmune rheumatic diseases (rheumatoid arthritis [RA] and systemic lupus erythematosus [SLE]).

To date, children and patients with autoimmune disease have rarely experienced progression of their infection to cytokine release syndrome, the third phase of coronavirus disease 2019 (COVID-19), with few being admitted to intensive care units.
also decline with age, and CD8+ T cells decline in number progressively with aging. Lymphocyte number and function is well known that IL-6 inhibits natural killer (NK) cell cytotoxicity. Therefore, IL-6 appears to be a key molecule.

In addition to the potential role of sex, we would like to speculate on the immunologic basis for rheumatic disease patients not having more severe outcomes, as might have been expected at the onset of this pandemic. In the early phases of infection, the lungs of patients with COVID-19 exhibit edema, a patchy inflammatory infiltrate, and multinucleated giant cells (MGCs), with lymphopenia in the peripheral blood. Evidence from animal models demonstrates that macrophage colony-stimulating factor and granulocyte-macrophage colony-stimulating factor stimulate the differentiation of rat alveolar macrophages into MGCs with distinct phenotypes (type 1 and type 2 MGC) and that neutralization of endogenous macrophage colony-stimulating factor and granulocyte–macrophage colony-stimulating factor before SARS–CoV-2 infection may enter type II alveolar epithelial cells (AECs) through angiotensin-converting enzyme 2 (ACE2) present on the membrane of type II AECs and employs serine protease TMPRSS2 for priming (7). Once type II AECs are infected, they provoke an innate immune response and synthesize type I interferon (IFNα/β), type II IFN (IFNγ), IL-6, and IL-8 (8). In the majority of patients with this response, the infection clears.

Initial phase of viral infection. In this phase, nonspecific viral agents (while specific agents are awaited), antimalarials, or anti–interleukin-6 (anti–IL-6) (or other anticytokine) agents may be used to shut down the inflammatory process before it evolves into acute respiratory distress syndrome–induced lung failure. SARS–CoV-2 = severe acute respiratory syndrome coronavirus 2; ACE2 = angiotensin-converting enzyme 2; IFNα/β = interferon α/β; TLR-7 = Toll-like receptor 7; ssRNA = single-stranded RNA; AT 2 = type II alveolar epithelial cells; Myd88 = myeloid differentiation factor 88; TNF = tumor necrosis factor; MCP-1 = monocyte chemotactic protein 1.
population. This is why scientific societies support the idea of continuing treatments (IL-6 inhibitors for juvenile idiopathic arthritis, DMARDs or JAK inhibitors for adult RA, and mycophenolate mofetil or HCQ for SLE). While specific antivirals are awaited, these drugs may help in the hyperinflammatory phase of the infection, and, in fact, several trials are underway using anti-IL-6, other cytokines, or JAK1/2 inhibitors (ClinicalTrials.gov). The key question is whether, or when, to prescribe glucocorticoids once the hyperinflammatory phase progresses to the cytokine release syndrome and ARDS-like phase. Data from clinical trials and the real world are badly needed to support these theories.

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Antiphospholipid syndrome is still a rare disease—estimated prevalence in the Piedmont and Aosta Valley regions of northwest Italy: comment on the article by Duarte-Garcia et al

To the Editor:

We read with interest the article by Duarte-Garcia et al (1), in which they reported that the estimated prevalence of antiphospholipid syndrome (APS) was 50 per 100,000 population. APS is an autoimmune disorder characterized by thrombotic events, pregnancy morbidity, or both, in the presence of antiphospholipid antibodies (aPLs) (2). While APS is often thought to be the most common thrombophilia, its global incidence and prevalence in the general population still need to be fully elucidated. Some reports describe an incidence of 5 cases per 100,000 population per year and a prevalence of 40–50 per 100,000 population (1,3–6). In several recent studies, investigators attempted to estimate the prevalence of aPLs in different cohorts, such as in young patients with stroke (7), patients with pregnancy morbidity, stroke, myocardial infarction, and deep vein thrombosis (4), and patients with a first unprovoked thrombosis (8). To date, APS meets the definition of a rare disease as described by Holué (prevalence ≤5 per 10,000 population) (9).

In order to better estimate the epidemiology of APS, we performed an analysis using a population-based approach, investigating clinicopeidemiologic data on patients with APS in northwest Italy. We collected data from the Piedmont and Aosta Valley Rare Disease Registry, part of the National Registry of Rare Diseases (10). The registry includes demographic, socioeconomic, and disease data, as detailed elsewhere (11) and currently includes 740 patients with a definite diagnosis of APS. The location of the centers reporting APS diagnoses by relative number of diagnoses is depicted in Figure 1. The median age at diagnosis was 45 years (interquartile range 23); 63% of patients were diagnosed at age ≤50 years, 39% at ≤40 years, and 18% at ≤30 years. Taking into account that the population of the Piedmont and Aosta Valley regions is ~4.4 million (12), the estimated prevalence of APS in the region is 1.68 per 10,000 population. The annual incidence from 2010 through 2019 was 1.1 per 100,000 population. APS is considered to be a rare disease according to the Rare Disease Registry of Piedmont and Aosta Valley. Despite the fact that the numbers are relatively small, an accurate estimation of the epidemiology of rare diseases is crucial in order to: 1) plan adequate strategies to maximize...