中文題目：僵直性脊椎炎病人使用生物製劑治療和空氣污染之相關

英文題目：Association between Air Pollutants and Initiation of Biological Therapy in Patients with Ankylosing Spondylitis

作　　者：高宗楸[2,3]，顏在弘[1,2,3]，陳韻文[1,2,3]，黃文男[2,3,4]，陳怡行[2,3,5]，吳明儒[3,5,6]，陳信華[1,2,3,5,7]

服務單位：[1]台中榮民總醫院 內科部一般內科，[2]台中榮民總醫院 內科部過敏免疫風濕科，[3]國立中興大學 醫學院學士後醫學系，[4]嶺東科技大學 企業管理系，[5]國立陽明交通大學 醫學院醫學系，[6]台中榮民總醫院 內科部，[7]國立中興大學 生命科學院榮興轉譯醫學研究中心 理學院大數據中心

Background: Ankylosing spondylitis (AS) is a common rheumatic disease characterized by chronic inflammatory arthritis and enthesitis involving spine and peripheral joints. The first line medical therapy includes non-steroidal anti-inflammatory drugs (NSAIDs) for spinal and peripheal joint involvement and conventional synthetic disease-modifying antirheumatic Drugs (csDMARDs), such as methotrexate (MTX) and sulfasalazine (SSZ), for peripheral arthritis . Biological therapy is indicated for patients with AS who do not have adequate response to first line therapy. Therefore, initiation of biologics such as tumor necrosis factor inhibitor (TNFi) and interleukin-17 inhibitor (IL-17i) may be used as a proxy to indicate high disease activity of AS. The related epidemiologic studies are still lacking currently. Outdoor air pollution had been found to trigger systemic inflammatory response, and therefore was a potential risk factor for high AS disease activity. We thus aim to investigate the association between air pollutants and initiation of biological therapy in patients with AS.

Methods: From AS patients as defined above, we excluded patients who had outpatient or inpatient visits with a diagnosis of rheumatoid arthritis (ICD-9-CM code 714.0) during 2003–2013. We also excluded who were treated with biologics including etanercept, adalimumab and golimumab before the first date of ambulatory or inpatient visit with a diagnosis of AS. We identified all AS patients who initiated biological therapy during 2012–2013 as the biologic group. The index date was the first date of biologics prescription. We matched the biologic group with AS patients who never received biological therapy during 2003–2013 at a 1:4 ratio for sex, birth year (± 3 years), year at first AS diagnosis, year at first biologic use and disease duration (± 0.3 year), and finally included 584 biologic users and 2,336 controls. We used the hourly level of ambient air pollutants across from 60 air quality censoring stations to

estimate the mean concentrations of air pollutants, including PM2.5, PM10, NO2, CO, SO2 and O3, within one year prior to the index date. We utilized graph convolutional neural network to assess the level of air pollutants at each residential location, and the level of ambient air pollutants at 374 residential locations in Taiwan was calculated according to the data of three air quality censoring stations near the location.

We examined the associations of biologic use air pollutants using conditional logistic regression analyses hown as adjusted odds ratio (aOR) with 95% confidence intervals (CIs) adjusting for potential confounders including age, disease duration, Charlson comorbidity index (CCI), level of insured amount, urbanization level, use of NSAIDs, use of methotrexate, use of sulfasalazine, the daily dosage of corticosteroids, and extra-articular manifestations (i.e., acute anterior uveitis [AAU], psoriasis and inflammatory bowel disease [IBD]

Results: The initiation of biologics was associated with disease duration (aOR, 8.97; 95% CI, 5.99–13.46), CCI (aOR, 1.31; 95% CI, 1.12–1.53), psoriasis (aOR, 25.06; 95% CI, 9.47–66.35), use of NSAIDs (aOR, 23.66; 95% CI, 8.96–62.46), use of MTX (aOR, 4.53; 95% CI, 2.93–7.00), use of SSZ (aOR, 12.15; 95% CI, 8.98–15.45), prednisolone equivalent dose (mg/day) (aOR, 1.11; 95% CI, 1.05-1.18), CO (per 1 ppm) (aOR, 8.58; 95% CI, 2.02–36.35) and NO2 (per 10 ppb) (aOR, 0.23; 95% CI, 0.11–0.50).

Conclusions: This nationwide, population-based study showed that initiation of biologics, a proxy of high disease activity, in patients with AS was associated positively with CO level, but negatively associated with NO2 level. Further clinical studies are warranted to confirm our findings. Mechanistical studies are also needed to elucidate the influence of CO and NO2 on the disease activity of AS.