**Title Characters: 190 (Title Character Limit 250)**

**Body Characters excluding title, authors, affiliations, conflicts: 2194 + 500 (fixed character count for each Table is 250) = Total characters 2694.**

**(Body Character Limit 2750 characters excluding title, authors, affiliations, conflicts)**

**Do TNF Inhibitors Reduce the Incidence and Prevalence of Comorbidities in Ankylosing Spondylitis (AS)?**

Atul Deodhar, Kevin Winthrop, Benjamin Chan, Sarah Siegel, Lisa Pisenti\*, Jeffery Stark\*, Robert Suruki\*, Rhonda L. Bohn\*, Huifeng Yun\*\*, Lang Chen\*\*, Jeffery Curtis\*\*.

Oregon Health & Science University, Portland, \*UCB Biosciences, \*\*University of Alabama, Birmingham.

**Background:** Patients with ankylosing spondylitis, a multi-system immune-mediated chronic inflammatory disease, have shown a reduction in signs and symptoms, improvement in physical function and quality of life with the advent of tumor necrosis factor inhibitors (TNFi) treatment. The magnitude of the impact of TNFi on the incidence of comorbidities in AS is not known.

**Methods:** Three commercial insurance claims databases (Multi-Payer Claims Database [MPCD 2007-2010], Truven MarketScan [2010-2014], and the US Medicare Fee-for-Service Claims data [2006-2014]) were searched to assess extra-articular manifestations (uveitis, psoriasis, inflammatory bowel disease) and comorbidities (cardiac, renal, pulmonary, neurologic) in three hierarchical exposure groups of AS patients: those(1) managed with either no therapy or prescription non-steroidal anti-inflammatory drugs (NSAIDs), (2) those on conventional disease modifying anti-rheumatic drugs (DMARDs), and (3) those prescribed TNFi. Entry criteria were a rheumatologist’s diagnosis of AS, six-months of pre-diagnosis insurance coverage, and administration of drug-specific exposures of interest after AS diagnosis. Prevalent comorbidities were identified from the period between AS cohort entry and treatment exposure. Incident comorbidities were identified from the period between treatment exposure and the earliest of date of death, loss of medical coverage, end of study period, first outcome occurrence, or treatment discontinuation or initiation of therapy at a higher level in exposure hierarchy.

**Results:** Total number of members included in the three databases is approximately 40 million. The prevalence of comorbidities and extra-articular manifestations of AS by treatment exposures, stratified by each data source, are shown in Table 1. The incidence rates of outcome of interest by treatment exposures, stratified by each data source, are shown in Table 2.

**Table 1:** Prevalence of comorbidities and extra-articular manifestations per 100 treatment exposures, stratified by data source.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Specific manifestation** | **MPCD** | | | **MarketScan** | | | **Medicare** | | |
| **TNFi** | **DMARDS** | **NSAIDS/**  **No Exposure** | **TNFi** | **DMARDS** | **NSAIDS/ No eExposure** | **TNFi** | **DMARDS** | **NSAIDS/ No Exposure** |
| Aortic Insufficiency | 1.5 | 0.8 | 2.0 | 1.8 | 2.1 | 2.8 | 8.0 | 10.9 | 11.7 |
| Conduction Block | 0.4 | 0.8 | 0.8 | 1.7 | 2.4 | 2.5 | 6.8 | 8.6 | 10.5 |
| Myocardial infarction | 0.3 | NA | 0.5 | 0.5 | 0.5 | 0.5 | 1.7 | 1.9 | 2.4 |
| Crohn’s Disease | 6.1 | 4.2 | 2.9 | 6.4 | 4.8 | 3.3 | 10.4 | 8.8 | 5.8 |
| Ulcerative Colitis | 3.7 | 3.1 | 2.0 | 4.9 | 3.0 | 2.6 | 7.4 | 7.2 | 4.9 |
| Amyloidosis | NA | NA | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.2 |
| IgA nephropathy | 0.1 | 0.2 | 0.1 | 0.2 | 0.2 | 0.1 | 0.7 | 0.9 | 0.6 |
| Nephrotic syndrome | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.2 | 0.5 | 0.3 |
| Apical Pulmonary fibrosis | NA | NA | 0.0 | 0.0 | NA | 0.0 | 0.0 | 0.1 | 0.0 |
| Interstitial lung disease | 0.2 | NA | 0.0 | 0.1 | 0.2 | 0.1 | 0.3 | 0.5 | 0.2 |
| Restrictive lung disease | 1.0 | 0.6 | 1.6 | 3.9 | 4.4 | 4.7 | 15.5 | 20.1 | 18.0 |
| Cauda Equina syndrome | NA | NA | 0.1 | 0.1 | 0.2 | 0.1 | 0.2 | 0.3 | 0.3 |
| Spinal Cord compression | 0.1 | NA | 0.3 | 0.3 | 0.5 | 0.5 | 1.7 | 2.0 | 2.4 |
| Psoriasis | 4.1 | 2.5 | 2.7 | 5.1 | 3.8 | 2.3 | 9.9 | 8.0 | 5.8 |
| Psoriatic arthritis | 6.6 | 4.8 | 2.4 | 8.5 | 6.2 | 2.9 | 13.9 | 10.1 | 5.4 |
| Uveitis | 11.3 | 8.5 | 7.4 | 13.4 | 11.0 | 11.2 | 13.4 | 10.1 | 8.0 |

**Table 2:** Crude Incidence Rates of comorbidities and disease manifestations per 100 patient-years by treatment exposures (TNFi versus NSAIDs/No treatment, or TNFi versus DMARDs), stratified by data source. Only significant data are shown.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MPCD Database** | | | **Marketscan Database** | | | **Medicare Database** | | |
|  | **TNFi** | **NSAIDs/No Treatment** | **p Value** | **TNFi** | **NSAIDs/No Treatment** | **p Value** | **TNFi** | **NSAIDs/No Treatmetn** | **p Value** |
| **Comparison of TNFi vs NSAIDs** | | | | | | | | | |
| **Aortic Insufficiency** | 1.3 | 1.9 | NS | 1.2 | 2.1 | 0.000 | 3.2 | 6.0 | 0.000 |
| **Conduction Block** | 0.3 | 0.9 | 0.03 | 1.1 | 2.4 | 0.000 | 2.9 | 5.9 | 0.000 |
| **Myocardial Infarction** | 0.3 | 0.6 | NS | 0.2 | 0.6 | 0.000 | 0.7 | 1.5 | 0.000 |
| **Restrictive Lung Disease** | 0.9 | 2.0 | 0.008 | 1.9 | 3.2 | 0.000 | 5.9 | 8.7 | 0.000 |
| **Spinal Cord Compression** | 0.1 | 0.3 | NS | 0.3 | 0.5 | 0.01 | 0.4 | 0.8 | 0.000 |
| **Psoriasis** | 3.5 | 1.6 | 0.000 | 3.8 | 1.8 | 0.000 | 3.8 | 2.1 | 0.000 |
| **Crohn’s Disease** | 4.7 | 3.0 | 0.006 | 4.8 | 2.6 | 0.000 | 3.9 | 2.5 | 0.000 |
| **Ulcerative Colitis** | 2.5 | 1.6 | 0.05 | 3.1 | 2.1 | 0.000 | 2.4 | 1.8 | 0.000 |
| **Uveitis** | 5.0 | 4.9 | NS | 7.6 | 8.0 | NS | 5.0 | 3.0 | 0.000 |
| **Comparison of TNFi vs DMARDs** | | | | | | | | | |
| **Aortic Insufficiency** | 1.3 | 0.5 | 0.132 | 1.2 | 1.5 | 0.279 | 3.2 | 4.7 | 0.000 |
| **Conduction Block** | 0.3 | 0.0 | 0.286 | 1.1 | 1.4 | 0.473 | 2.9 | 4.2 | 0.000 |
| **Myocardial Infarction** | 0.3 | 0.0 | 0.286 | 0.2 | 0.3 | 0.568 | 0.7 | 1.2 | 0.000 |
| **Restrictive Lung Disease** | 0.9 | 0.0 | 0.029 | 1.9 | 2.4 | 0.190 | 5.9 | 7.7 | 0.000 |
| **Psoriasis** | 3.5 | 1.0 | 0.003 | 3.8 | 3.3 | 0.397 | 3.8 | 3.4 | 0.161 |
| **Ulcerative Colitis** | 2.5 | 0.9 | 0.041 | 3.1 | 3.2 | 0.816 | 2.4 | 2.6 | 0.472 |
| **Uveitis** | 5.0 | 6.5 | 0.228 | 7.6 | 8.6 | 0.200 | 5.0 | 3.8 | 0.000 |

**Conclusion**: This is the largest investigation of the prevalence of comorbidities and extra-articular manifestations of AS within the US, using three insurance claims databases. Patients treated with TNFi have lower incidence of certain cardiac, pulmonary and neurologic comorbidities compared to those treated with NSAIDs or DMARDs alone, but higher incidence of some extra-articular manifestations (e.g. psoriasis, uveitis and IBD) where TNFi may be implicated.

**CONFLICTS:**

AD has received research grants from Amgen, Eli Lilly, GSK, Janssen, Novartis, UCB; and has served on the advisory boards of Eli Lilly, Janssen, Novartis, UCB.

RLB is a Contractor for UCB and Owner of Bohn Epidemiology, LLC. There are no conflicts with other clients.