The Landscape of Real-world Research of Treatment Patterns and Clinical Outcomes in Patients Treated with Adalimumab: A Scoping Review

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BACKGROUND

- Adalimumab is a fully human monoclonal antibody and is a tumor necrosis factor alpha (TNFα) inhibitor indicated for use in the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), psoriasis (PsO), juvenile idiopathic arthritis (JIA), ulcerative colitis (UC), hidradenitis suppurativa (HS), and uveitis (UV) [1]
- Since its initial approval in 2002, 10 biosimilars have entered the market but many barriers to patient access still exist [2]
- There is a lack of real-world utilization and effectiveness outcomes for adalimumab products

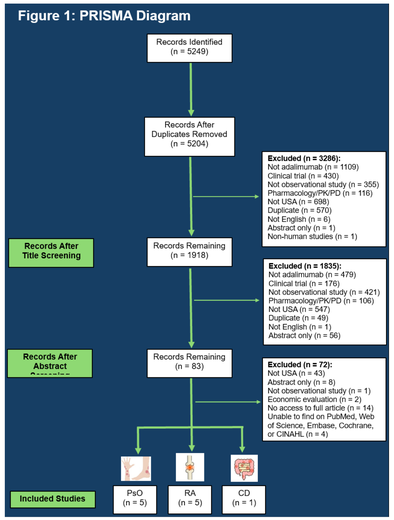
OBJECTIVE

- To develop a comprehensive understanding of observational research and real-world evidence (RWE) evaluating adalimumab use and its biosimilars

METHODS

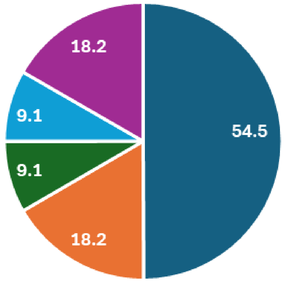
- Scoping review conducted according to the PRISMA-ScR framework (Figure 1)
- Peer-reviewed articles published in English anytime up to July 4th, 2023, were included
- Included studies were observational (prospective or retrospective), conducted in the United States, and included patients aged 18 years or older treated with adalimumab for any approved or off-label indication
- Data were descriptively analyzed and summarized based on overall trends, similarities, and differences across included studies and stratified by disease state

Figure 1: PRISMA Diagram



RESULTS

Figure 2: Studies' Data Sources



Claims Data (n = 6, 54.5%)
Registries (n = 2, 18.2%)
Encounters Database (n = 2, 18.2%)
Supplemental Database (n = 1, 9.1%)
Pharmacy Benefits Manager (n = 1, 9.1%)

* One study utilized both claims and encounters data and is accounted for twice in Figure 2.

Of the 11 studies that met the inclusion criteria, the average sample size was 2,091 patients.

Citation	Article Title	Outcome measures	Findings
Bagel J, et al. *J Med Econ.* 2021;24(1):782-791	Dose escalation and associated costs in biologic treatment of psoriasis based on real-world data	Above-label use, dose escalation, duration of above-label use, and associated costs.	Of 4,141 patients receiving adalimumab, 513 were above label. Mean time to above label use was 99.5 days. Median duration of above label use was just below 150 days. Labeled use resulted in $50,569 and above label use resulted in $61,102 all cause costs.
Blume SW, et al. *Adv Ther.* 2013;30(5):517-527	Tumor necrosis factor-blocker dose escalation in rheumatoid arthritis patients in a pharmacy benefit management setting	Duration, persistence, and dose escalation rates.	Of 852 patients on adalimumab; 45.9% were new starts. Patients receiving ADA had significantly higher rates of dose escalation than those receiving ETA. New starts dose escalation rates were 8.3–14.1%. For continuing patients, rates ranged from 7.0–28.3%.
Delate T, et al. *J Manag Care Spec Pharm.* 2017;23(8):798-808.	Patterns of Care for Biologic-Dosing Outliers and Nonoutliers in Biologic-Naive Patients with Rheumatoid Arthritis	Prevalence of low-dose and high-dose outliers by index biologic.	ADA patients were most likely to become outliers. Of all outliers during the 1-year follow-up, patients were more likely to be a high-dose outlier (55%) than a low-dose outlier (45%). Total biologic costs were highest for ADA and ETA nonoutliers.
Doshi JA, et al. *J Am Acad Dermatol.* 2016;74(6):1057-1065.	Biologic therapy adherence, discontinuation, switching, and restarting among patients with psoriasis in the US Medicare population	Adherence, discontinuation, switching, and restarting of the index biologic.	We examined 1,083 patients initiating adalimumab. 40.7% were adherent, 43.4% discontinued, 9.0% switched, 6.6% restarted (5.1% with index, 1.5% with different biologic).
Feldman SR, et al. *J Manag Care Spec Pharm.* 2015;21(3):201-209.	Patterns of medication utilization and costs associated with the use of etanercept, adalimumab, and ustekinumab in the management of moderate-to-severe psoriasis	Dose escalation, switching, restarting, or discontinuation.	Of the 1,681 patients on adalimumab 37% escalated doses, 27% discontinued within 12 months, 10% restarted the same biologic, and 10% switched to another biologic. The persistence rate over 12 months was 53%.
Feldman SR, et al. *J Dermatolog Treat.* 2021;32(2):203-211.	Real-world treatment patterns and healthcare costs of biologics and apremilast among patients with moderate-to-severe plaque psoriasis by metabolic condition status	Adherence, non-persistence, discontinuation, re-initiation, switching, combination therapy, and total costs.	Patients with metabolic conditions had higher discontinuation and switching rates while on adalimumab; 53.9% vs. 48.7% and 47.8% vs. 41.9%, respectively. Patients with metabolic conditions incurred significantly higher costs.
Harrold LR, et al. *J Rheumatol.* 2020;47(7):959-967.	Long-term, real-world safety of adalimumab in rheumatoid arthritis	Serious infections, malignancies, CHF requiring hospitalization, TB, drug-induced SLE, and mortality.	Incidence per 100 person-years for serious infections, CHF hospitalizations, malignancies, and mortality were 1.86, 0.15, 0.64, and 0.33, respectively. The risk of serious infection was highest in the first year of therapy. The median time to discontinuation was 11 months, while the median time to first serious infection was 12 months.
Khilfeh I, et al. *J Manag Care Spec Pharm.* 2019;25(4):461-467.	Adherence, Persistence, and Expenditures for High-Cost Anti-Inflammatory Drugs in Rheumatoid Arthritis: An Exploratory Study	Adherence, persistence, switch rates, and direct medical costs	ADA (n = 226) was the second most used medication. Concurrent MTX use was associated with higher persistence (+307 days with ADA). The most commonly switched-to drug after ADA was abatacept (n = 39).
Edward V., et al. *Journal of Crohn's and Colitis.* 2011; 5(6): 550–554	Adalimumab real-world dosage pattern and predictors of weekly dosing: patients with Crohn's disease in the United States	Mean of age, duration of follow up, sex, dose, region.	1,335 patients received ADA as maintenance therapy. Mean age of the sample was 41 (±14) years and duration of follow up was 253 (±111) days. 58% were women, 85% had received adalimumab 160/80 mg as induction therapy, and 55% were from Southern USA.
Pappas DA, et al. *Rheumatol Ther.* 2017;4(2):375-389.	Long-Term Effectiveness of Adalimumab in Patients with Rheumatoid Arthritis: An Observational Analysis from the Corrona Rheumatoid Arthritis Registry	Patient demographics, clinical characteristics, persistency, disease activity, functionality	Of the 1,791 ADA new starts, persistence of at least 1 and 12 years was 64.1% and 10.2%, respectively. 67% of those persisting at least 1 year (77.1% female, mean age 53.9 years) were in remission with clinically meaningful improvements. 61.6% of those who discontinued were not in remission and 41.9% switched biologic within 12 months after discontinuing.
Xu C, et al. *J Dermatolog Treat.* 2022;33(4):2270-2277.	Treatment adherence and persistence of seven commonly prescribed biologics for moderate to severe psoriasis and psoriatic arthritis in a U.S. commercially insured population	Adherence and persistence	During the 9-month follow-up period, the proportion of patients with PDC 80% was 48.6%. The proportion of patients who were persistent with their index biologic (ADA) during the 9-month follow-up period was 30.7%.

REFERENCES

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A complete list of studies that were included in this research may be found via this QR code.

ACKNOWLEDGEMENTS

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CONCLUSIONS

- Most studied disease states are psoriasis and arthritis; most RWE studies are designed retrospectively and are used to assess adherence, persistence, discontinuation, switching, and restarting of adalimumab products in the United States using mainly claims data from a variety of data sources
- In general, studies found that adalimumab was more likely than other products to have dose escalation or to be used above label, increasing the risk of infections, and first occurring on average around 12 months from start of therapy. Time to discontinuation was about 12 months, and persistence past 12 months was around 50%
- Majority of studies are funded by pharmaceutical manufacturers
- These findings will help identify potential gaps in literature which can inform future studies

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