TNF Inhibitors: Prevalence of Use and Predictors of Treatment Non-Persistence in the 2011-2016 Medicare Population

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Background/Purpose

- Tumor necrosis factor inhibitors (TNFis) are commonly used to treat inflammatory disease in patients with inadequate response to conventional therapies.
- **Objectives**: Using a contemporary database of Medicare beneficiaries, we aimed to:
  1. Characterize the use of TNFis, and
  2. Investigate factors associated with non-persistence to TNFis in those with diagnosed rheumatoid arthritis.

Methods

- **Data source**: Administrative claims records for a 20% sample of Medicare beneficiaries from 2010-2016.
- **Study population**: New-users of TNFi therapy.
- **TNFi therapy**: Identified using Part D prescription or Part B injectable/IV drug claims.
- **TNFi non-persistence**: Defined as a gap in supply of the index TNFi of more than 180 days.
- **Baseline characteristics**: Defined using claims in year preceding the index TNFi claim. Comorbid conditions were defined based on diagnosis in ≥ 1 inpatient or ≥ 2 outpatient claims separated by ≥ 30 days.
- **Inclusion criteria**:
  - One or more claims for TNFi therapy, 2011-2016.
  - Medicare Parts A/B and D coverage for at least 1 year prior to the date of the first (index) TNFi claim.
- **Exclusion criteria**:
  - Prior use of TNFi therapy (in 2010).
  - Fewer than 2 TNFi claims or no diagnosis for rheumatoid arthritis (non-persistence analysis only).
- **Statistical analysis**: Multivariable Cox proportional hazards regression was used to assess factors associated with TNFi non-persistence.

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Results

- We identified 15,622 new-users of TNFis (Table 1).
- Mean age was 64 ± 13 years, and 71% were female.
- History of rheumatoid arthritis (60%) was the most common indication, and 40% of patients had baseline concomitant use of conventional DMARDs and corticosteroids.
- Of 8,147 rheumatoid arthritis patients, only 20-30% remained persistent to the index TNFi by 5 years (Fig 2, Table 2).

Table 1. Baseline characteristics of Medicare patients initiating TNFi therapy, 2010-2016

	Adalimumab N = 4,669	Certolizumab pegol N = 1,705	Etanercept N = 3,190	Golimumab N = 1,015	Infliximab N = 5,043	Total N = 15,622
Age, mean ± SD years	60 ± 14	69 ± 11	62 ± 13	69 ± 11	67 ± 12	64 ± 13
Age category, %						
< 45 years	15.8	4.6	12.0	4.0	6.5	10.0
45-64 years	36.3	15.5	37.2	17.0	17.9	27.0
65-74 years	33.6	51.1	35.3	52.0	53.0	43.3
75-84 years	12.3	24.0	13.4	23.4	19.9	17.0
85+ years	1.9	4.8	2.1	3.4	2.7	2.6
Female, %	68.5	78.0	72.7	75.7	68.6	70.9
Race, %						
White	77.4	86.2	77.8	85.7	86.3	81.8
Black	12.2	6.9	11.3	8.6	8.2	9.9
Other race	10.4	6.9	10.8	5.7	5.5	8.2
Indicated diseases, %*						
Rheumatoid arthritis	45.0	79.7	66.7	91.2	56.7	60.0
Psoriatic arthritis	8.4	10.0	11.0	5.7	9.5	9.3
Ankylosing spondylitis	2.6	2.5	2.9	1.5	3.7	3.0
Crohn's disease	15.7	7.0	0.4	< 1.1	16.4	10.9
Ulcerative colitis	7.1	1.4	0.6	2.3	12.4	6.5
Plaque psoriasis	21.1	5.6	20.0	3.7	6.9	13.5
Hidradenitis suppurativa	1.9	< 0.6	< 0.3	< 1.1	0.4	< 0.8
Uveitis	0.4	< 0.6	< 0.3	< 1.1	0.6	< 0.4
Co-medications, %						
Conventional DMARDs	32.9	44.2	42.4	55.3	40.9	40.1
Non-TNF biologics	0.4	2.3	1.0	4.7	1.7	1.4
Corticosteroids	33.3	43.2	38.3	47.0	48.9	41.3
Comorbid conditions, %						
Myocardial infarction	2.7	2.1	3.4	2.3	3.4	3.0
Congestive heart failure	6.7	6.7	8.2	6.6	6.4	6.9
PVD	7.3	9.9	7.6	7.4	8.2	8.0
Cerebrovascular disease	5.0	5.9	5.7	5.4	6.2	5.7
COPD	22.6	21.8	25.4	19.4	21.9	22.6
Liver disease	4.8	4.1	5.9	3.4	4.6	4.8
Renal disease	7.9	9.5	8.7	8.8	8.8	8.6
Cancer	4.5	5.9	4.8	6.2	6.6	5.5
Diabetes	29.7	23.2	31.3	25.7	25.8	27.8
Hypertension	56.5	62.5	59.2	63.9	60.7	59.6

COPD: chronic obstructive pulmonary disease, DMARD: disease-modifying antirheumatic drug, PVD: peripheral vascular disease, SD: standard deviation, TNFi: tumor necrosis factor inhibitor

*Frequencies shown in gray if disease not indicated for a specific TNFi drug

- Female sex, COPD, and hypertension were associated with a higher rate of non-persistence, and concomitant DMARD use was associated with a lower rate of non-persistence (Fig 1).
- Compared with infliximab use, rates of non-persistence were higher among users of adalimumab, certolizumab pegol, and etanercept, and lower among users of golimumab (Fig 1).

Figure 1. Hazard ratios (HR) and 95% confidence intervals (CI) for non-persistence to the index TNFi among 8,147 Medicare patients with a diagnosis of rheumatoid arthritis and at least 2 TNFi claims, 2011-2016

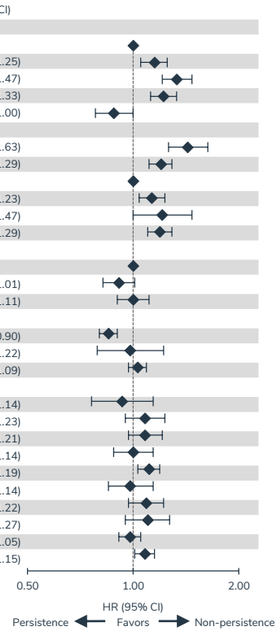

Figure 2. Kaplan-Meier survival curves for time to non-persistence to the index TNFi among 8147 Medicare patients with a diagnosis of rheumatoid arthritis and at least 2 TNFi claims, 2011-2016.

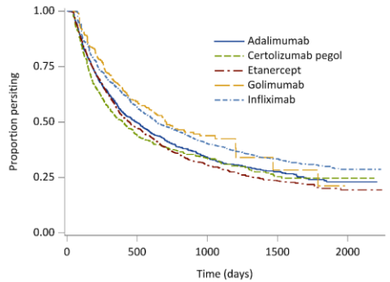

Table 2. Proportion (%) remaining persistent to the index TNFi over follow-up

	1 year	2 years	3 years	4 years	5 years
Adalimumab	57.0	40.8	31.9	27.9	24.1
Certolizumab pegol	51.4	37.9	31.9	26.5	24.7
Etanercept	56.2	37.3	28.8	23.7	20.1
Golimumab	67.0	48.8	42.5	34.0	21.2
Infliximab	65.1	47.4	38.9	33.6	30.0

Conclusion

- TNFIs are used in a diverse set of Medicare beneficiaries.
- In rheumatoid arthritis patients, the rate of persistence varied by sex, age, co-medication with DMARDs, comorbid disease, and the type of TNFi.
- Potential reasons for differences in persistence to TNFis
  - Drug effectiveness and safety
  - Patient characteristics:
    - health status (residual confounding)
    - drug administration preference
- Medicare 20% Part B/D data are a valuable resource for investigating drug use in routine clinical practice (frequencies, costs, persistence/adherence, effectiveness).