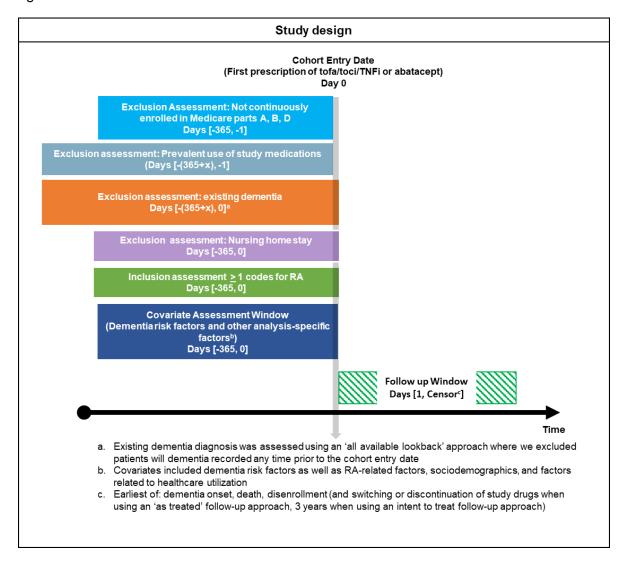
Supplemental Online Content

Desai RJ, Varma VR, Gerhard T, et al. Comparative risk of Alzheimer disease and related dementia among Medicare beneficiaries with rheumatoid arthritis treated with targeted disease-modifying antirheumatic agents. *JAMA Netw Open.* 2022;5(4):e226567. doi:10.1001/jamanetworkopen.2022.6567

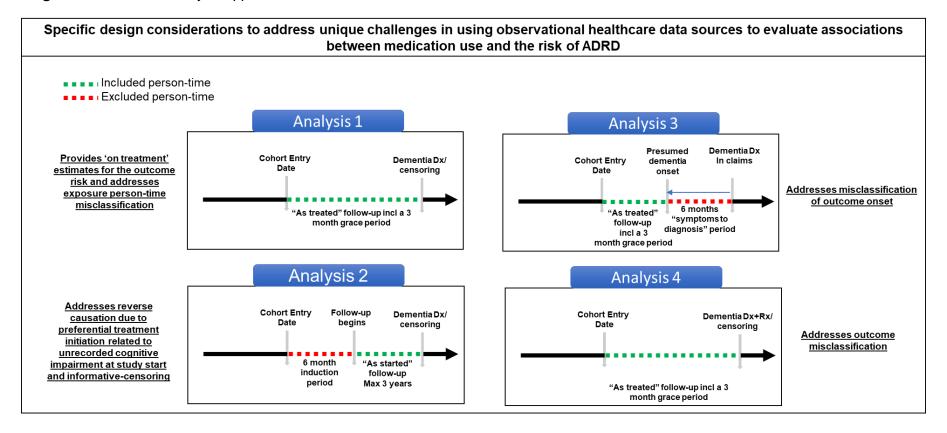
- eFigure 1. Study Design
- eFigure 2. Alternative Analytic Approaches
- **eFigure 3.** Patient Attrition Flowchart
- **eFigure 4.** Risk of Alzheimer Disease and Related Dementia in Patients Treated With Tofacitinib, Tocilizumab, or TNF Inhibitors vs Abatacept Before Propensity Score Matching
- **eFigure 5.** Subgroup Analyses Risk of Alzheimer Disease and Related Dementia in Patients Treated With Tofacitinib vs Abatacept After Propensity Score Matching Within Each Subgroup
- **eFigure 6.** Subgroup Analyses Risk of Alzheimer Disease and Related Dementia in Patients Treated With Tocilizumab vs Abatacept After Propensity Score Matching Within Each Subgroup
- **eFigure 7.** Subgroup Analyses Risk of Alzheimer Disease and Related Dementia in Patients Treated With TNF Inhibitors vs Abatacept After Propensity Score Matching Within Each Subgroup
- **eTable 1.** Codes Used to Identify Alzheimer Disease and Related Dementia From Medicare Claims
- **eTable 2.** Baseline Characteristics of Patients Included in the Study Cohort Before Propensity Score Matching
- **eTable 3.** Baseline Characteristics of Patients Included in the Study Cohort After 1:1 Propensity Score Matching
- **eTable 4.** Results for Alzheimer Disease in Patients Treated With Targeted Disease Modifying Antirheumatic Drugs

This supplemental material has been provided by the authors to give readers additional information about their work.

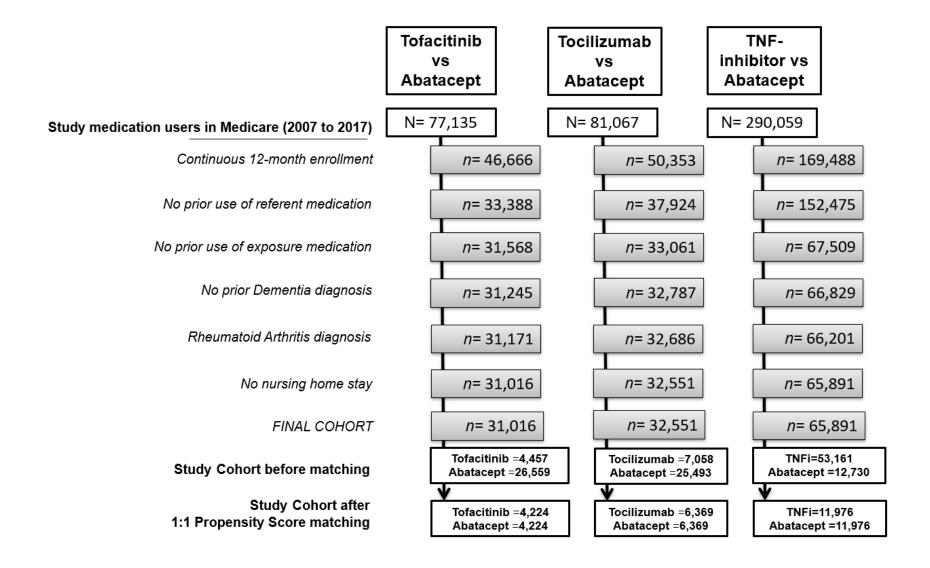
eFigure 1. Study Design



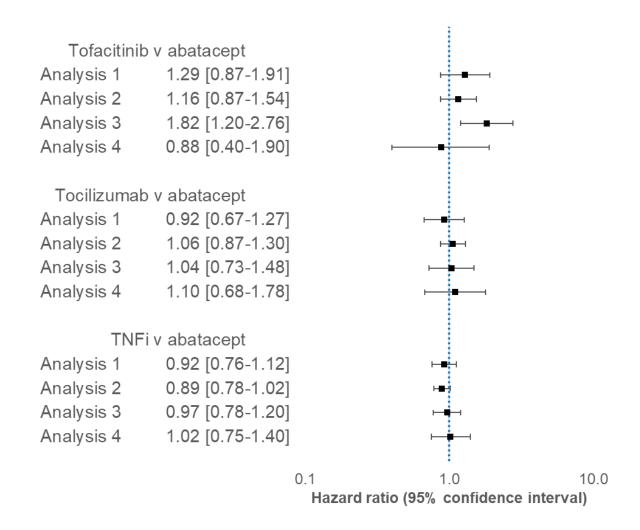
eFigure 2. Alternative Analytic Approaches



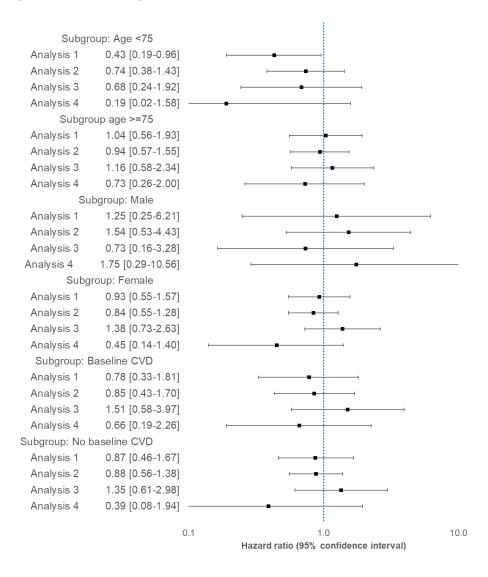
eFigure 3. Patient Attrition Flowchart



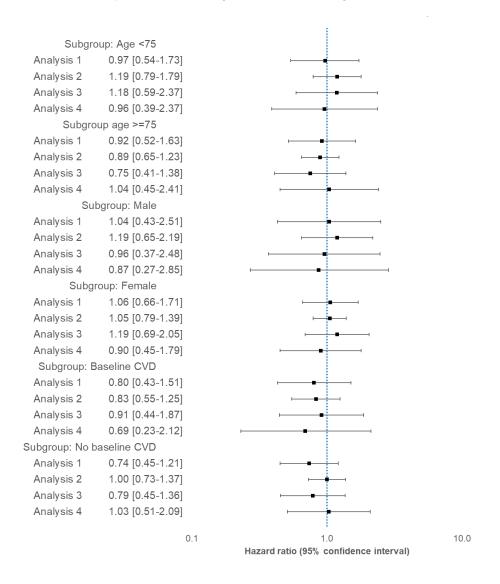
eFigure 4. Risk of Alzheimer Disease and Related Dementia in Patients Treated With Tofacitinib, Tocilizumab, or TNF Inhibitors vs Abatacept Before Propensity Score Matching



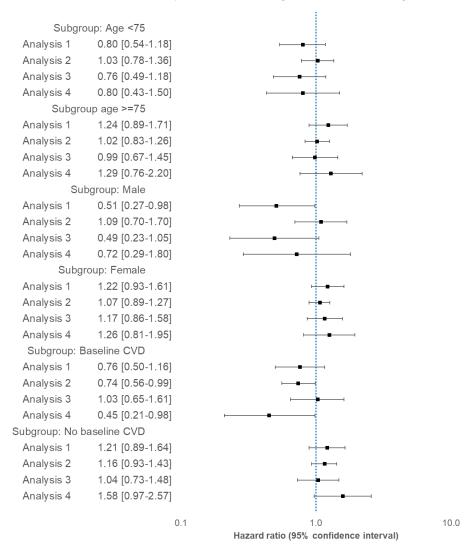
eFigure 5. Subgroup Analyses Risk of Alzheimer Disease and Related Dementia in Patients Treated With Tofacitinib vs Abatacept After Propensity Score Matching Within Each Subgroup



eFigure 6. Subgroup Analyses Risk of Alzheimer Disease and Related Dementia in Patients Treated With Tocilizumab vs Abatacept After Propensity Score Matching Within Each Subgroup



eFigure 7. Subgroup Analyses Risk of Alzheimer Disease and Related Dementia in Patients Treated With TNF Inhibitors vs Abatacept After Propensity Score Matching Within Each Subgroup



eTable 1. Codes Used to Identify Alzheimer Disease and Related Dementia From Medicare Claims

Condition	ICD-9 and ICD-10 codes
Alzheimer's disease	331.0*, F00*, G30*
Vascular dementia	290.4*, F01*
Senile, presenile, or unspecified dementia	290.0*, 290.1*. 290.3*, 797*, F03*
Dementia in other diseases classified	331.1*, 331.2*, 331.7*, 294.1*, F02*
elsewhere	

eTable 2. Baseline Characteristics of Patients Included in the Study Cohort Before Propensity Score Matching

Variable*	Tofacitinib	Abatacept	St. Diff	Tocilizumab	Abatacept	St. Diff	TNF inhibitors	Abatacept	St. Diff
	(N = 4,456)	(N = 25,008)		(N = 6,411)	(N = 24,021)		(N = 51,013)	(N = 12,000)	
Demographics									
Age, mean (SD)	72.11 (5.69)	72.55 (5.81)	-0.08	72.05 (5.52)	72.56 (5.83)	-0.09	71.98 (5.70)	72.67 (5.93)	-0.12
Gender, n (%)									
Male	778 (17.5%)	4,426 (17.7%)	-0.01	1,349 (21.0%)	4,248 (17.7%)	0.08	11,675 (22.9%)	2,136 (17.8%)	0.13
Female	3,678 (82.5%)	20,582 (82.3%)	0.01	5,062 (79.0%)	19,773 (82.3%)	-0.08	39,338 (77.1%)	9,864 (82.2%)	-0.13
Race, n (%)									
White	3,572 (80.2%)	21,940 (87.7%)	-0.21	5,662 (88.3%)	21,030 (87.5%)	0.02	43,140 (84.6%)	10,438 (87.0%)	-0.07
Black	488 (11.0%)	1,506 (6.0%)	0.18	373 (5.8%)	1,468 (6.1%)	-0.01	4,012 (7.9%)	791 (6.6%)	0.05
Asian	96 (2.2%)	311 (1.2%)	0.08	64 (1.0%)	307 (1.3%)	-0.03	893 (1.8%)	154 (1.3%)	0.04
Hispanic	138 (3.1%)	675 (2.7%)	0.02	148 (2.3%)	657 (2.7%)	-0.03	1,493 (2.9%)	344 (2.9%)	0
Native American	30 (0.7%)	116 (0.5%)	0.03	32 (0.5%)	117 (0.5%)	0	401 (0.8%)	44 (0.4%)	0.05
Other	89 (2.0%)	326 (1.3%)	0.05	90 (1.4%)	315 (1.3%)	0.01	767 (1.5%)	174 (1.5%)	0
Unknown	43 (1.0%)	134 (0.5%)	0.06	42 (0.7%)	127 (0.5%)	0.03	307 (0.6%)	55 (0.5%)	0.01
Region, n (%)									
Northeast	1,029 (23.1%)	3,665 (14.7%)	0.22	1,059 (16.5%)	3,555 (14.8%)	0.05	8,838 (17.3%)	1,785 (14.9%)	0.07
South	1,834 (41.2%)	11,410 (45.6%)	-0.09	2,761 (43.1%)	10,938 (45.5%)	-0.05	21,973 (43.1%)	5,608 (46.7%)	-0.07
North Central	720 (16.2%)	5,277 (21.1%)	-0.13	1,172 (18.3%)	5,078 (21.1%)	-0.07	10,303 (20.2%)	2,452 (20.4%)	0
West	869 (19.5%)	4,598 (18.4%)	0.03	1,418 (22.1%)	4,392 (18.3%)	0.09	9,801 (19.2%)	2,120 (17.7%)	0.04
Unknown	<11	58 (0.2%)	-0.03	<11	58 (0.2%)	-0.06	98 (0.2%)	35 (0.3%)	-0.02
Calendar year of index date, n (%)									
2007	0 (0.0%)	2,057 (8.2%)	-0.42	0 (0.0%)	2,057 (8.6%)	-0.43	4,156 (8.1%)	870 (7.2%)	0.03
2008	0 (0.0%)	1,814 (7.3%)	-0.4	0 (0.0%)	1,814 (7.6%)	-0.41	3,294 (6.5%)	775 (6.5%)	0
2009	0 (0.0%)	2,136 (8.5%)	-0.43	0 (0.0%)	2,136 (8.9%)	-0.44	4,129 (8.1%)	971 (8.1%)	0
2010	0 (0.0%)	1,959 (7.8%)	-0.41	62 (1.0%)	1,958 (8.2%)	-0.35	4,122 (8.1%)	948 (7.9%)	0.01
2011	0 (0.0%)	1,848 (7.4%)	-0.4	755 (11.8%)	1,807 (7.5%)	0.15	4,326 (8.5%)	913 (7.6%)	0.03
2012	15 (0.3%)	2,249 (9.0%)	-0.42	574 (9.0%)	2,153 (9.0%)	0	4,423 (8.7%)	1,038 (8.6%)	0
2013	486 (10.9%)	2,223 (8.9%)	0.07	804 (12.5%)	2,089 (8.7%)	0.12	4,609 (9.0%)	1,087 (9.1%)	0

2014	850 (19.1%)	2,133 (8.5%)	0.31	907 (14.1%)	1,996 (8.3%)	0.18	5,003 (9.8%)	1,026 (8.6%)	0.04
2015	958 (21.5%)	2,627 (10.5%)	0.3	987 (15.4%)	2,457 (10.2%)	0.16	5,983 (11.7%)	1,388 (11.6%)	0.01
	` '			, ,			,	•	
2016	903 (20.3%)	2,808 (11.2%)	0.25	1,043 (16.3%)	2,610 (10.9%)	0.16	5,089 (10.0%)	1,405 (11.7%)	-0.05
2017	1,244 (27.9%)	3,154 (12.6%)	0.39	1,279 (20.0%)	2,944 (12.3%)	0.21	5,879 (11.5%)	1,579 (13.2%)	-0.05
Low income subsidy, n (%)	1,600 (35.9%)	4,409 (17.6%)	0.42	972 (15.2%)	4,360 (18.2%)	-0.08	12,357 (24.2%)	2,103 (17.5%)	0.17
Dementia risk factors, n (%)									
Diabetes	1,411 (31.7%)	7,583 (30.3%)	0.03	1,894 (29.5%)	7,319 (30.5%)	-0.02	16,183 (31.7%)	3,868 (32.2%)	-0.01
Obesity	851 (19.1%)	3,385 (13.5%)	0.15	1,115 (17.4%)	3,180 (13.2%)	0.12	6,927 (13.6%)	1,688 (14.1%)	-0.01
Hypertension	3,452 (77.5%)	19,114 (76.4%)	0.03	4,869 (75.9%)	18,346 (76.4%)	-0.01	39,242 (76.9%)	9,380 (78.2%)	-0.03
Coronary artery disease	1,166 (26.2%)	6,837 (27.3%)	-0.02	1,690 (26.4%)	6,580 (27.4%)	-0.02	13,221 (25.9%)	3,494 (29.1%)	-0.07
Depression	933 (20.9%)	4,678 (18.7%)	0.06	1,264 (19.7%)	4,437 (18.5%)	0.03	9,149 (17.9%)	2,317 (19.3%)	-0.04
Anxiety	769 (17.3%)	3,243 (13.0%)	0.12	907 (14.1%)	3,070 (12.8%)	0.04	6,564 (12.9%)	1,559 (13.0%)	0
Bipolar disorder	49 (1.1%)	241 (1.0%)	0.01	73 (1.1%)	232 (1.0%)	0.01	597 (1.2%)	108 (0.9%)	0.03
Schizophrenia	16 (0.4%)	33 (0.1%)	0.06	<11	31 (0.1%)	0	137 (0.3%)	16 (0.1%)	0.04
Markers for healthy behavior, frailty, healthcare use									
Smoking, n (%)	1,187 (26.6%)	4,485 (17.9%)	0.21	1,500 (23.4%)	4,222 (17.6%)	0.14	9,287 (18.2%)	2,213 (18.4%)	-0.01
Mammography, n (%)	1,488 (33.4%)	8,205 (32.8%)	0.01	2,197 (34.3%)	7,835 (32.6%)	0.04	15,150 (29.7%)	3,896 (32.5%)	-0.06
Colonoscopy, n (%)	452 (10.1%)	3,146 (12.6%)	-0.08	849 (13.2%)	3,002 (12.5%)	0.02	6,910 (13.5%)	1,524 (12.7%)	0.02
Fecal occult blood test, n (%)	383 (8.6%)	2,401 (9.6%)	-0.03	604 (9.4%)	2,313 (9.6%)	-0.01	4,952 (9.7%)	1,180 (9.8%)	0
Influenza vaccination, n (%)	2,928 (65.7%)	17,111 (68.4%)	-0.06	4,438 (69.2%)	16,425 (68.4%)	0.02	33,271 (65.2%)	8,140 (67.8%)	-0.06
Pneumococcal vaccination, n (%)	1,819 (40.8%)	6,599 (26.4%)	0.31	2,225 (34.7%)	6,259 (26.1%)	0.19	13,107 (25.7%)	3,275 (27.3%)	-0.04
Herpes zoster vaccination, n (%)	32 (0.7%)	122 (0.5%)	0.03	22 (0.3%)	122 (0.5%)	-0.03	357 (0.7%)	77 (0.6%)	0.01
Bone mineral density test, n (%)	1,103 (24.8%)	7,761 (31.0%)	-0.14	1,863 (29.1%)	7,473 (31.1%)	-0.04	14,879 (29.2%)	3,890 (32.4%)	-0.07
Number of distinct generic agents, mean (SD)	15.99 (7.23)	14.51 (6.69)	0	14.47 (6.73)	14.52 (6.71)	0	14.23 (6.77)	14.50 (6.63)	0
Number of emergency room visits, mean (SD)	0.69 (1.38)	0.65 (1.18)	0	0.64 (1.21)	0.65 (1.19)	0	0.62 (1.32)	0.67 (1.22)	0
Number of outpatient visits, mean (SD)	18.73 (19.02)	20.75 (17.93)	0	20.27 (16.84)	20.71 (18.06)	0	19.16 (18.07)	20.78 (17.93)	0
Number of hospitalizations, mean (SD)	0.31 (0.84)	0.36 (0.79)	0	0.32 (0.72)	0.36 (0.79)	0	0.30 (0.71)	0.37 (0.81)	0
Number of physician office visits, mean (SD)	4.92 (9.57)	5.53 (8.58)	0	5.02 (8.91)	5.57 (8.81)	0	5.53 (9.70)	5.70 (9.07)	0

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Number of rheumatologist visits, mean (SD)	4.39 (3.15)	5.44 (4.06)	0	5.53 (4.00)	5.38 (4.03)	0	4.43 (3.45)	4.99 (3.73)	0
Number of C-reactive protein tests ordered, mean (SD)	2.56 (2.29)	2.79 (2.70)	0	3.40 (2.99)	2.73 (2.66)	0	2.42 (2.36)	2.66 (2.54)	0
Number of serum creatinine tests ordered, mean (SD)	5.81 (3.38)	6.59 (3.62)	0	6.78 (3.66)	6.52 (3.58)	0	5.84 (3.38)	6.44 (3.70)	0
Composite frailty score, mean (SD)	0.17 (0.04)	0.17 (0.04)	0	0.17 (0.04)	0.17 (0.04)	0	0.16 (0.04)	0.17 (0.04)	0
Osteoporosis, n (%)	1,734 (38.9%)	10,744 (43.0%)	-0.08	2,622 (40.9%)	10,290 (42.8%)	-0.04	18,694 (36.6%)	5,286 (44.0%)	-0.15
Fractures, n (%)	499 (11.2%)	2,762 (11.0%)	0.01	700 (10.9%)	2,646 (11.0%)	0	5,169 (10.1%)	1,415 (11.8%)	-0.05
Falls, n (%)	215 (4.8%)	1,188 (4.8%)	0	305 (4.8%)	1,135 (4.7%)	0	2,239 (4.4%)	556 (4.6%)	-0.01
Use of supplemental oxygen, n (%)	101 (2.3%)	322 (1.3%)	0.08	121 (1.9%)	298 (1.2%)	0.06	516 (1.0%)	169 (1.4%)	-0.04
Combined comorbidity score, mean (SD)	1.59 (2.24)	1.58 (2.23)	0	1.58 (2.21)	1.58 (2.23)	0	1.40 (2.13)	1.74 (2.32)	0
Comedication use, n (%)									
Lithium	<11	24 (0.1%)	0.03	<11	<11	0	82 (0.2%)	<11	0.03
Anti-epileptic mood stabilizers	68 (1.5%)	315 (1.3%)	0.02	100 (1.6%)	296 (1.2%)	0.03	643 (1.3%)	152 (1.3%)	0
Anti-epileptics (other than mood stabilizers)	1,261 (28.3%)	6,063 (24.2%)	0.09	1,642 (25.6%)	5,788 (24.1%)	0.03	11,175 (21.9%)	3,050 (25.4%)	-0.08
Atypical antipsychotics	110 (2.5%)	368 (1.5%)	0.07	105 (1.6%)	344 (1.4%)	0.02	856 (1.7%)	186 (1.6%)	0.01
Benzodiazepines	978 (21.9%)	3,068 (12.3%)	0.26	1,140 (17.8%)	2,843 (11.8%)	0.17	5,916 (11.6%)	1,621 (13.5%)	-0.06
Serotonin-norepinephrine reuptake inhibitors	626 (14.0%)	2,818 (11.3%)	0.08	772 (12.0%)	2,666 (11.1%)	0.03	5,152 (10.1%)	1,362 (11.3%)	-0.04
Selective serotonin reuptake inhibitors	879 (19.7%)	5,133 (20.5%)	-0.02	1,362 (21.2%)	4,907 (20.4%)	0.02	10,074 (19.7%)	2,502 (20.8%)	-0.03
Tricyclic antidepressants	268 (6.0%)	1,883 (7.5%)	-0.06	466 (7.3%)	1,794 (7.5%)	-0.01	3,410 (6.7%)	893 (7.4%)	-0.03
Typical antipsychotics	<11	52 (0.2%)	0	12 (0.2%)	51 (0.2%)	0	111 (0.2%)	34 (0.3%)	-0.02
Anticoagulants	472 (10.6%)	2,718 (10.9%)	-0.01	721 (11.2%)	2,596 (10.8%)	0.01	4,724 (9.3%)	1,405 (11.7%)	-0.08
Antiplatelet agents	367 (8.2%)	2,204 (8.8%)	-0.02	499 (7.8%)	2,136 (8.9%)	-0.04	4,303 (8.4%)	1,114 (9.3%)	-0.03
Angiotensin II receptor blockers	1,137 (25.5%)	5,856 (23.4%)	0.05	1,533 (23.9%)	5,603 (23.3%)	0.01	11,477 (22.5%)	2,845 (23.7%)	-0.03
Angiotensin converting enzyme inhibitors	1,182 (26.5%)	7,120 (28.5%)	-0.04	1,745 (27.2%)	6,876 (28.6%)	-0.03	14,943 (29.3%)	3,443 (28.7%)	0.01
Beta blockers	1,777 (39.9%)	9,906 (39.6%)	0.01	2,520 (39.3%)	9,528 (39.7%)	-0.01	19,237 (37.7%)	4,972 (41.4%)	-0.08
Calcium channel blockers	1,313 (29.5%)	6,972 (27.9%)	0.04	1,732 (27.0%)	6,698 (27.9%)	-0.02	14,241 (27.9%)	3,373 (28.1%)	0
Diuretics	1,397 (31.4%)	8,277 (33.1%)	-0.04	2,046 (31.9%)	7,952 (33.1%)	-0.03	15,876 (31.1%)	4,113 (34.3%)	-0.07
Nitrates	298 (6.7%)	1,775 (7.1%)	-0.02	404 (6.3%)	1,718 (7.2%)	-0.04	3,344 (6.6%)	918 (7.6%)	-0.04
Lipid lowering drugs	2,245 (50.4%)	11,919 (47.7%)	0.05	3,178 (49.6%)	11,391 (47.4%)	0.04	24,485 (48.0%)	5,877 (49.0%)	-0.02

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Non-insulin diabetes medications	752 (16.9%)	3,880 (15.5%)	0.04	1,023 (16.0%)	3,735 (15.5%)	0.01	8,902 (17.5%)	1,904 (15.9%)	0.04
Insulin	307 (6.9%)	1,484 (5.9%)	0.04	403 (6.3%)	1,432 (6.0%)	0.01	3,371 (6.6%)	762 (6.3%)	0.01
Antidepressants	1,776 (39.9%)	9,580 (38.3%)	0.03	2,575 (40.2%)	9,135 (38.0%)	0.05	18,253 (35.8%)	4,631 (38.6%)	-0.06
Rheumatoid arthritis related factors									
Number of combined biologic DMARDs, n (%)									
0	1,532 (34.4%)	8,780 (35.1%)	-0.01	1,732 (27.0%)	8,779 (36.5%)	-0.21	42,333 (83.0%)	8,779 (73.2%)	0.24
1	1,578 (35.4%)	11,711 (46.8%)	-0.23	3,019 (47.1%)	11,510 (47.9%)	-0.02	6,475 (12.7%)	2,135 (17.8%)	-0.14
2	922 (20.7%)	3,566 (14.3%)	0.17	1,220 (19.0%)	3,050 (12.7%)	0.17	1,386 (2.7%)	795 (6.6%)	-0.19
3 or more	424 (9.5%)	951 (3.8%)	0.23	440 (6.9%)	682 (2.8%)	0.19	819 (1.6%)	291 (2.4%)	-0.06
Number of combined nonbiologic DMARDs, n (%)									
0	420 (9.4%)	2,363 (9.4%)	0	649 (10.1%)	2,289 (9.5%)	0.02	5,392 (10.6%)	1,056 (8.8%)	0.06
1	1,613 (36.2%)	10,332 (41.3%)	-0.1	2,679 (41.8%)	9,944 (41.4%)	0.01	22,286 (43.7%)	4,627 (38.6%)	0.1
2	1,398 (31.4%)	7,573 (30.3%)	0.02	1,883 (29.4%)	7,268 (30.3%)	-0.02	15,346 (30.1%)	3,809 (31.7%)	-0.03
3 or more	1,025 (23.0%)	4,740 (19.0%)	0.1	1,200 (18.7%)	4,520 (18.8%)	0	7,989 (15.7%)	2,508 (20.9%)	-0.13
Use of other nonbiologic DMARDs, n (%)	868 (19.5%)	4,432 (17.7%)	0.05	1,020 (15.9%)	4,270 (17.8%)	-0.05	8,912 (17.5%)	2,383 (19.9%)	-0.06
Methotrexate, n (%)	2,279 (51.1%)	14,395 (57.6%)	-0.13	3,458 (53.9%)	13,906 (57.9%)	-0.08	33,462 (65.6%)	7,005 (58.4%)	0.15
Hydroxychloroquine, n (%)	1,095 (24.6%)	5,885 (23.5%)	0.03	1,277 (19.9%)	5,710 (23.8%)	-0.09	13,001 (25.5%)	3,484 (29.0%)	-0.08
Leflunomide, n (%)	953 (21.4%)	4,742 (19.0%)	0.06	1,154 (18.0%)	4,585 (19.1%)	-0.03	8,563 (16.8%)	2,501 (20.8%)	-0.1
Nonsteroidal anti- inflammatory drugs/Coxibs, n (%)	1,578 (35.4%)	8,423 (33.7%)	0.04	2,059 (32.1%)	8,124 (33.8%)	-0.04	20,621 (40.4%)	4,123 (34.4%)	0.12
Opioids, n (%)	3,033 (68.1%)	18,062 (72.2%)	-0.09	4,574 (71.3%)	17,320 (72.1%)	-0.02	35,170 (68.9%)	8,764 (73.0%)	-0.09
Glucocorticoids use/dose, n (%)	3,292 (73.9%)	18,512 (74.0%)	0	4,945 (77.1%)	17,784 (74.0%)	0.07	36,429 (71.4%)	8,961 (74.7%)	-0.07
Comorbid conditions, n (%)									
Atrial fibrillation	464 (10.4%)	2,908 (11.6%)	-0.04	744 (11.6%)	2,797 (11.6%)	0	4,797 (9.4%)	1,544 (12.9%)	-0.11
Heart failure	543 (12.2%)	3,212 (12.8%)	-0.02	751 (11.7%)	3,103 (12.9%)	-0.04	5,226 (10.2%)	1,711 (14.3%)	-0.13
Stroke or transient ischemic attack	360 (8.1%)	2,233 (8.9%)	-0.03	606 (9.5%)	2,144 (8.9%)	0.02	4,116 (8.1%)	1,090 (9.1%)	-0.04
Peripheral vascular disease	570 (12.8%)	3,051 (12.2%)	0.02	718 (11.2%)	2,952 (12.3%)	-0.03	5,913 (11.6%)	1,586 (13.2%)	-0.05
Hyperlipidemia	2,978 (66.8%)	16,683 (66.7%)	0	4,425 (69.0%)	15,979 (66.5%)	0.05	34,197 (67.0%)	8,217 (68.5%)	-0.03
Renal dysfunction	748 (16.8%)	3,774 (15.1%)	0.05	1,051 (16.4%)	3,610 (15.0%)	0.04	6,871 (13.5%)	1,996 (16.6%)	-0.09

Chronic liver disease	374 (8.4%)	2,402 (9.6%)	-0.04	573 (8.9%)	2,280 (9.5%)	-0.02	4,605 (9.0%)	1,247 (10.4%)	-0.05
Asthma	1,003 (22.5%)	4,028 (16.1%)	0.16	1,266 (19.7%)	3,843 (16.0%)	0.1	8,100 (15.9%)	1,996 (16.6%)	-0.02
Ischemic heart disease	1,135 (25.5%)	6,650 (26.6%)	-0.03	1,635 (25.5%)	6,403 (26.7%)	-0.03	12,876 (25.2%)	3,403 (28.4%)	-0.07
Chronic obstructive pulmonary disease	1,213 (27.2%)	6,165 (24.7%)	0.06	1,750 (27.3%)	5,906 (24.6%)	0.06	12,405 (24.3%)	3,042 (25.4%)	-0.03
Malignancy	926 (20.8%)	6,219 (24.9%)	-0.1	1,691 (26.4%)	5,947 (24.8%)	0.04	11,474 (22.5%)	3,033 (25.3%)	-0.07
Drug or alcohol abuse or dependence	535 (12.0%)	1,795 (7.2%)	0.16	609 (9.5%)	1,705 (7.1%)	0.09	4,317 (8.5%)	925 (7.7%)	0.03
Venous thromboembolism	261 (5.9%)	1,453 (5.8%)	0	381 (5.9%)	1,383 (5.8%)	0	2,499 (4.9%)	768 (6.4%)	-0.07

^{*} Numbers <11 are suppressed according to Data Use Agreement with the Centers for Medicare and Medicare Services

eTable 3. Baseline Characteristics of Patients Included in the Study Cohort After 1:1 Propensity Score Matching

Variable*	Tofacitinib	Abatacept	St. Diff	Tocilizumab	Abatacept	St. Diff	TNF inhibitors	Abatacept	St. Diff
	(N = 4,224)	(N = 4,224)		(N = 6,369)	(N = 6,369)		(N = 11,976)	(N = 11,976)	
Demographics									
Age, mean (SD)	72.18 (5.70)	72.19 (5.59)	0	72.05 (5.53)	71.99 (5.38)	0.01	72.68 (5.90)	72.67 (5.92)	0
Gender, n (%)									
Male	751 (17.8%)	752 (17.8%)	0	1,333 (20.9%)	1,300 (20.4%)	0.01	2,106 (17.6%)	2,136 (17.8%)	-0.01
Female	3,473 (82.2%)	3,472 (82.2%)	0	5,036 (79.1%)	5,069 (79.6%)	-0.01	9,870 (82.4%)	9,840 (82.2%)	0.01
Race, n (%)									
White	3,408 (80.7%)	3,401 (80.5%)	0.01	5,624 (88.3%)	5,627 (88.3%)	0	10,413 (86.9%)	10,414 (87.0%)	0
Black	442 (10.5%)	434 (10.3%)	0.01	371 (5.8%)	365 (5.7%)	0	813 (6.8%)	791 (6.6%)	0.01
Asian	92 (2.2%)	97 (2.3%)	-0.01	64 (1.0%)	65 (1.0%)	0	142 (1.2%)	154 (1.3%)	-0.01
Hispanic	132 (3.1%)	137 (3.2%)	-0.01	148 (2.3%)	148 (2.3%)	0	349 (2.9%)	344 (2.9%)	0
Native American	27 (0.6%)	28 (0.7%)	-0.01	32 (0.5%)	35 (0.5%)	0	38 (0.3%)	44 (0.4%)	-0.02
Other	82 (1.9%)	90 (2.1%)	-0.01	89 (1.4%)	90 (1.4%)	0	176 (1.5%)	174 (1.5%)	0
Unknown	41 (1.0%)	37 (0.9%)	0.01	41 (0.6%)	39 (0.6%)	0	45 (0.4%)	55 (0.5%)	-0.01
Region, n (%)									
Northeast	951 (22.5%)	944 (22.3%)	0	1,053 (16.5%)	1,050 (16.5%)	0	1,765 (14.7%)	1,781 (14.9%)	-0.01
South	1,754 (41.5%)	1,775 (42.0%)	-0.01	2,748 (43.1%)	2,743 (43.1%)	0	5,616 (46.9%)	5,597 (46.7%)	0
North Central	692 (16.4%)	657 (15.6%)	0.02	1,168 (18.3%)	1,169 (18.4%)	0	2,439 (20.4%)	2,448 (20.4%)	0
West	823 (19.5%)	843 (20.0%)	-0.01	1,399 (22.0%)	1,405 (22.1%)	0	2,114 (17.7%)	2,115 (17.7%)	0
Unknown	<11	<11	0	<11	<11	0	42 (0.4%)	35 (0.3%)	0.02
Calendar year of index date, n (%)									
2007	0 (0.0%)	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	0	874 (7.3%)	870 (7.3%)	0
2008	0 (0.0%)	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	0	784 (6.5%)	775 (6.5%)	0
2009	0 (0.0%)	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	0	958 (8.0%)	969 (8.1%)	0
2010	0 (0.0%)	0 (0.0%)	0	62 (1.0%)	64 (1.0%)	0	972 (8.1%)	944 (7.9%)	0.01
2011	0 (0.0%)	0 (0.0%)	0	750 (11.8%)	748 (11.7%)	0	925 (7.7%)	912 (7.6%)	0
2012	15 (0.4%)	17 (0.4%)	0	574 (9.0%)	566 (8.9%)	0	1,073 (9.0%)	1,036 (8.7%)	0.01
2013	475 (11.2%)	481 (11.4%)	-0.01	802 (12.6%)	776 (12.2%)	0.01	1,113 (9.3%)	1,085 (9.1%)	0.01

2014	807 (19.1%)	831 (19.7%)	-0.02	898 (14.1%)	920 (14.4%)	-0.01	1,006 (8.4%)	1,026 (8.6%)	-0.01
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2015	907 (21.5%)	908 (21.5%)	0	979 (15.4%)	974 (15.3%)	0	1,353 (11.3%)	1,387 (11.6%)	-0.01
2016	859 (20.3%)	840 (19.9%)	0.01	1,035 (16.3%)	1,047 (16.4%)	0	1,399 (11.7%)	1,401 (11.7%)	0
2017	1,161 (27.5%)	1,147 (27.2%)	0.01	1,269 (19.9%)	1,274 (20.0%)	0	1,519 (12.7%)	1,571 (13.1%)	-0.01
Low income subsidy, n (%)	1,396 (33.0%)	1,383 (32.7%)	0.01	966 (15.2%)	974 (15.3%)	0	2,080 (17.4%)	2,103 (17.6%)	-0.01
Dementia risk factors, n (%)									
Diabetes	1,338 (31.7%)	1,329 (31.5%)	0	1,886 (29.6%)	1,859 (29.2%)	0.01	3,884 (32.4%)	3,857 (32.2%)	0
Obesity	808 (19.1%)	812 (19.2%)	0	1,102 (17.3%)	1,084 (17.0%)	0.01	1,720 (14.4%)	1,685 (14.1%)	0.01
Hypertension	3,269 (77.4%)	3,276 (77.6%)	0	4,843 (76.0%)	4,833 (75.9%)	0	9,357 (78.1%)	9,358 (78.1%)	0
Coronary artery disease	1,111 (26.3%)	1,138 (26.9%)	-0.01	1,680 (26.4%)	1,632 (25.6%)	0.02	3,447 (28.8%)	3,479 (29.0%)	0
Depression	876 (20.7%)	855 (20.2%)	0.01	1,256 (19.7%)	1,286 (20.2%)	-0.01	2,336 (19.5%)	2,306 (19.3%)	0.01
Anxiety	717 (17.0%)	706 (16.7%)	0.01	900 (14.1%)	913 (14.3%)	-0.01	1,541 (12.9%)	1,556 (13.0%)	0
Bipolar disorder	44 (1.0%)	53 (1.3%)	-0.03	72 (1.1%)	75 (1.2%)	-0.01	98 (0.8%)	107 (0.9%)	-0.01
Schizophrenia	<11	12 (0.3%)	-0.02	<11	<11	0	15 (0.1%)	16 (0.1%)	0
Markers for healthy behavior, frailty, healthcare use									
Smoking, n (%)	1,116 (26.4%)	1,130 (26.8%)	-0.01	1,491 (23.4%)	1,478 (23.2%)	0	2,188 (18.3%)	2,206 (18.4%)	0
Mammography, n (%)	1,415 (33.5%)	1,390 (32.9%)	0.01	2,185 (34.3%)	2,204 (34.6%)	-0.01	3,875 (32.4%)	3,887 (32.5%)	0
Colonoscopy, n (%)	434 (10.3%)	412 (9.8%)	0.02	841 (13.2%)	837 (13.1%)	0	1,513 (12.6%)	1,519 (12.7%)	0
Fecal occult blood test, n (%)	367 (8.7%)	369 (8.7%)	0	597 (9.4%)	615 (9.7%)	-0.01	1,171 (9.8%)	1,177 (9.8%)	0
Influenza vaccination, n (%)	2,791 (66.1%)	2,772 (65.6%)	0.01	4,412 (69.3%)	4,454 (69.9%)	-0.01	8,092 (67.6%)	8,120 (67.8%)	0
Pneumococcal vaccination, n (%)	1,717 (40.6%)	1,701 (40.3%)	0.01	2,208 (34.7%)	2,226 (35.0%)	-0.01	3,138 (26.2%)	3,263 (27.2%)	-0.02
Herpes zoster vaccination, n (%)	25 (0.6%)	26 (0.6%)	0	22 (0.3%)	31 (0.5%)	-0.03	77 (0.6%)	77 (0.6%)	0
Bone mineral density test, n (%)	1,060 (25.1%)	1,092 (25.9%)	-0.02	1,853 (29.1%)	1,860 (29.2%)	0	3,863 (32.3%)	3,882 (32.4%)	0
Number of distinct generic agents, mean (SD)	15.81 (7.11)	15.95 (7.40)	0	14.48 (6.72)	14.43 (6.63)	0	14.52 (6.70)	14.49 (6.62)	0
Number of emergency room visits, mean (SD)	0.69 (1.37)	0.70 (1.28)	0	0.64 (1.21)	0.63 (1.16)	0	0.67 (1.25)	0.67 (1.22)	0
Number of outpatient visits, mean (SD)	18.77 (19.30)	18.95 (14.06)	0	20.22 (16.82)	20.23 (16.90)	0	20.83 (19.19)	20.73 (17.76)	0
Number of hospitalizations, mean (SD)	0.31 (0.84)	0.31 (0.73)	0	0.32 (0.72)	0.31 (0.72)	0	0.37 (0.80)	0.37 (0.81)	0
Number of physician office visits, mean (SD)	4.92 (9.75)	5.00 (6.31)	0	5.03 (8.93)	5.05 (8.77)	0	5.76 (10.01)	5.69 (9.04)	0

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Number of rheumatologist visits, mean (SD)	4.44 (3.16)	4.49 (3.14)	0	5.49 (3.88)	5.46 (4.02)	0	4.96 (4.01)	4.98 (3.69)	0
Number of C-reactive protein tests ordered, mean (SD)	2.59 (2.30)	2.61 (2.34)	0	3.35 (2.92)	3.35 (2.87)	0	2.63 (2.57)	2.66 (2.54)	0
Number of serum creatinine tests ordered, mean (SD)	5.87 (3.42)	5.95 (3.18)	0	6.76 (3.65)	6.72 (3.53)	0	6.43 (3.81)	6.43 (3.70)	0
Composite frailty score, mean (SD)	0.17 (0.04)	0.17 (0.04)	0	0.17 (0.04)	0.17 (0.04)	0	0.17 (0.05)	0.17 (0.04)	0
Osteoporosis, n (%)	1,637 (38.8%)	1,669 (39.5%)	-0.01	2,605 (40.9%)	2,588 (40.6%)	0.01	5,300 (44.3%)	5,268 (44.0%)	0.01
Fractures, n (%)	465 (11.0%)	499 (11.8%)	-0.03	698 (11.0%)	671 (10.5%)	0.02	1,384 (11.6%)	1,409 (11.8%)	-0.01
Falls, n (%)	207 (4.9%)	205 (4.9%)	0	304 (4.8%)	291 (4.6%)	0.01	569 (4.8%)	555 (4.6%)	0.01
Use of supplemental oxygen, n (%)	90 (2.1%)	77 (1.8%)	0.02	119 (1.9%)	112 (1.8%)	0.01	169 (1.4%)	167 (1.4%)	0
Combined comorbidity score, mean (SD)	1.60 (2.26)	1.61 (2.25)	0	1.58 (2.21)	1.53 (2.19)	0	1.72 (2.34)	1.73 (2.31)	0
Comedication use, n (%)									
Lithium	<11	<11	0	<11	<11	0	13 (0.1%)	<11	0
Anti-epileptic mood stabilizers	64 (1.5%)	73 (1.7%)	-0.02	95 (1.5%)	101 (1.6%)	-0.01	155 (1.3%)	152 (1.3%)	0
Anti-epileptics (other than mood stabilizers)	1,187 (28.1%)	1,192 (28.2%)	0	1,630 (25.6%)	1,621 (25.5%)	0	2,996 (25.0%)	3,032 (25.3%)	-0.01
Atypical antipsychotics	93 (2.2%)	93 (2.2%)	0	105 (1.6%)	101 (1.6%)	0	192 (1.6%)	185 (1.5%)	0.01
Benzodiazepines	920 (21.8%)	935 (22.1%)	-0.01	1,125 (17.7%)	1,120 (17.6%)	0	1,583 (13.2%)	1,613 (13.5%)	-0.01
Serotonin-norepinephrine reuptake inhibitors	583 (13.8%)	581 (13.8%)	0	768 (12.1%)	775 (12.2%)	0	1,383 (11.5%)	1,357 (11.3%)	0.01
Selective serotonin reuptake inhibitors	835 (19.8%)	818 (19.4%)	0.01	1,351 (21.2%)	1,384 (21.7%)	-0.01	2,444 (20.4%)	2,494 (20.8%)	-0.01
Tricyclic antidepressants	252 (6.0%)	256 (6.1%)	0	460 (7.2%)	453 (7.1%)	0	884 (7.4%)	890 (7.4%)	0
Typical antipsychotics	<11	<11	0	12 (0.2%)	14 (0.2%)	0	28 (0.2%)	33 (0.3%)	-0.02
Anticoagulants	449 (10.6%)	455 (10.8%)	-0.01	718 (11.3%)	709 (11.1%)	0.01	1,365 (11.4%)	1,397 (11.7%)	-0.01
Antiplatelet agents	346 (8.2%)	351 (8.3%)	0	495 (7.8%)	500 (7.9%)	0	1,118 (9.3%)	1,110 (9.3%)	0
Angiotensin II receptor blockers	1,079 (25.5%)	1,078 (25.5%)	0	1,522 (23.9%)	1,556 (24.4%)	-0.01	2,882 (24.1%)	2,840 (23.7%)	0.01
Angiotensin converting enzyme inhibitors	1,115 (26.4%)	1,133 (26.8%)	-0.01	1,737 (27.3%)	1,740 (27.3%)	0	3,417 (28.5%)	3,436 (28.7%)	0
Beta blockers	1,690 (40.0%)	1,717 (40.6%)	-0.01	2,506 (39.3%)	2,464 (38.7%)	0.01	4,878 (40.7%)	4,954 (41.4%)	-0.01
Calcium channel blockers	1,242 (29.4%)	1,213 (28.7%)	0.02	1,721 (27.0%)	1,726 (27.1%)	0	3,399 (28.4%)	3,369 (28.1%)	0.01
Diuretics	1,329 (31.5%)	1,329 (31.5%)	0	2,036 (32.0%)	1,963 (30.8%)	0.03	4,114 (34.4%)	4,097 (34.2%)	0
Nitrates	283 (6.7%)	294 (7.0%)	-0.01	401 (6.3%)	376 (5.9%)	0.02	906 (7.6%)	911 (7.6%)	0
Lipid lowering drugs	2,125 (50.3%)	2,191 (51.9%)	-0.03	3,159 (49.6%)	3,136 (49.2%)	0.01	5,860 (48.9%)	5,865 (49.0%)	0

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Non-insulin diabetes medications	710 (16.8%)	682 (16.1%)	0.02	1,017 (16.0%)	1,014 (15.9%)	0	1,928 (16.1%)	1,901 (15.9%)	0.01
Insulin	290 (6.9%)	290 (6.9%)	0	402 (6.3%)	388 (6.1%)	0.01	785 (6.6%)	759 (6.3%)	0.01
Antidepressants	1,677 (39.7%)	1,665 (39.4%)	0.01	2,557 (40.1%)	2,570 (40.4%)	-0.01	4,590 (38.3%)	4,617 (38.6%)	-0.01
Rheumatoid arthritis related factors									
Number of combined biologic DMARDs, n (%)									
0	1,454 (34.4%)	1,417 (33.5%)	0.02	1,726 (27.1%)	1,686 (26.5%)	0.01	8,791 (73.4%)	8,776 (73.3%)	0
1	1,513 (35.8%)	1,514 (35.8%)	0	3,007 (47.2%)	3,027 (47.5%)	-0.01	2,148 (17.9%)	2,130 (17.8%)	0
2	866 (20.5%)	873 (20.7%)	0	1,211 (19.0%)	1,245 (19.5%)	-0.01	749 (6.3%)	779 (6.5%)	-0.01
3 or more	391 (9.3%)	420 (9.9%)	-0.02	425 (6.7%)	411 (6.5%)	0.01	288 (2.4%)	291 (2.4%)	0
Number of combined nonbiologic DMARDs, n (%)									
0	396 (9.4%)	416 (9.8%)	-0.01	642 (10.1%)	622 (9.8%)	0.01	1,079 (9.0%)	1,055 (8.8%)	0.01
1	1,542 (36.5%)	1,494 (35.4%)	0.02	2,657 (41.7%)	2,678 (42.0%)	-0.01	4,723 (39.4%)	4,624 (38.6%)	0.02
2	1,312 (31.1%)	1,311 (31.0%)	0	1,875 (29.4%)	1,885 (29.6%)	0	3,679 (30.7%)	3,800 (31.7%)	-0.02
3 or more	974 (23.1%)	1,003 (23.7%)	-0.01	1,195 (18.8%)	1,184 (18.6%)	0.01	2,495 (20.8%)	2,497 (20.9%)	0
Use of other nonbiologic DMARDs, n (%)	817 (19.3%)	875 (20.7%)	-0.04	1,017 (16.0%)	1,033 (16.2%)	-0.01	2,390 (20.0%)	2,379 (19.9%)	0
Methotrexate, n (%)	2,168 (51.3%)	2,129 (50.4%)	0.02	3,435 (53.9%)	3,381 (53.1%)	0.02	6,930 (57.9%)	7,002 (58.5%)	-0.01
Hydroxychloroquine, n (%)	1,038 (24.6%)	1,070 (25.3%)	-0.02	1,275 (20.0%)	1,275 (20.0%)	0	3,452 (28.8%)	3,477 (29.0%)	0
Leflunomide, n (%)	902 (21.4%)	888 (21.0%)	0.01	1,151 (18.1%)	1,193 (18.7%)	-0.02	2,471 (20.6%)	2,492 (20.8%)	0
Nonsteroidal anti- inflammatory drugs/Coxibs, n (%)	1,474 (34.9%)	1,472 (34.8%)	0	2,050 (32.2%)	2,022 (31.7%)	0.01	4,127 (34.5%)	4,119 (34.4%)	0
Opioids, n (%)	2,870 (67.9%)	2,877 (68.1%)	0	4,544 (71.3%)	4,502 (70.7%)	0.01	8,799 (73.5%)	8,742 (73.0%)	0.01
Glucocorticoids use/dose, n (%)	3,127 (74.0%)	3,099 (73.4%)	0.01	4,913 (77.1%)	4,877 (76.6%)	0.01	8,880 (74.1%)	8,943 (74.7%)	-0.01
Comorbid conditions, n (%)									
Atrial fibrillation	451 (10.7%)	435 (10.3%)	0.01	741 (11.6%)	720 (11.3%)	0.01	1,514 (12.6%)	1,528 (12.8%)	-0.01
Heart failure	522 (12.4%)	526 (12.5%)	0	748 (11.7%)	697 (10.9%)	0.03	1,748 (14.6%)	1,696 (14.2%)	0.01
Stroke or transient ischemic attack	343 (8.1%)	343 (8.1%)	0	600 (9.4%)	599 (9.4%)	0	1,098 (9.2%)	1,086 (9.1%)	0
Peripheral vascular disease	542 (12.8%)	537 (12.7%)	0	715 (11.2%)	696 (10.9%)	0.01	1,589 (13.3%)	1,578 (13.2%)	0
Hyperlipidemia	2,824 (66.9%)	2,834 (67.1%)	0	4,390 (68.9%)	4,344 (68.2%)	0.02	8,165 (68.2%)	8,199 (68.5%)	-0.01
Renal dysfunction	721 (17.1%)	723 (17.1%)	0	1,044 (16.4%)	1,034 (16.2%)	0.01	1,972 (16.5%)	1,986 (16.6%)	0

Chronic liver disease	361 (8.5%)	362 (8.6%)	0	571 (9.0%)	561 (8.8%)	0.01	1,224 (10.2%)	1,238 (10.3%)	0
Asthma	940 (22.3%)	939 (22.2%)	0	1,253 (19.7%)	1,252 (19.7%)	0	1,985 (16.6%)	1,987 (16.6%)	0
Ischemic heart disease	1,080 (25.6%)	1,103 (26.1%)	-0.01	1,626 (25.5%)	1,576 (24.7%)	0.02	3,348 (28.0%)	3,388 (28.3%)	-0.01
Chronic obstructive pulmonary disease	1,135 (26.9%)	1,111 (26.3%)	0.01	1,733 (27.2%)	1,752 (27.5%)	-0.01	2,986 (24.9%)	3,031 (25.3%)	-0.01
Malignancy	901 (21.3%)	904 (21.4%)	0	1,674 (26.3%)	1,698 (26.7%)	-0.01	3,093 (25.8%)	3,023 (25.2%)	0.01
Drug or alcohol abuse or dependence	490 (11.6%)	480 (11.4%)	0.01	606 (9.5%)	627 (9.8%)	-0.01	916 (7.6%)	924 (7.7%)	0
Venous thromboembolism	243 (5.8%)	249 (5.9%)	0	381 (6.0%)	382 (6.0%)	0	796 (6.6%)	762 (6.4%)	0.01

^{*} Numbers <11 are suppressed according to Data Use Agreement with the Centers for Medicare and Medicare Services

eTable 4. Results for Alzheimer Disease in Patients Treated With Targeted Disease Modifying Antirheumatic Drugs

Analysis scheme*	Exposure	N of patients	N outcomes†	N person years	Avg follow- up (years)	Incidence rate (95% CI)/1,000 py	Hazard Ratio (95%CI)
Tofacitinib vs abatace	ept						
Analysis 1	Tofacitinib	4,224	<11	3,471	0.8	2.02 (0.81-4.16)	
	Abatacept	4,224	<11	3,994	0.9	2.00 (0.86-3.95)	1.06 (0.38, 2.93)
Analysis 2	Tofacitinib	2,164	11	3,393	1.6	3.24 (1.62-5.80)	
	Abatacept	2,164	12	3,521	1.6	3.41 (1.76-5.95)	0.97 (0.43, 2.19)
Analysis 3	Tofacitinib	2,053	<11	2,032	1.0	3.44 (1.38-7.10)	
	Abatacept	2,053	<11	2,063	1.0	1.94 (0.53-4.96)	1.80 (0.53-6.16)
Analysis 4	Tofacitinib	4,224	<11	3,472	0.8	1.73 (0.63-3.76)	
	Abatacept	4,224	<11	3,996	0.9	1.00 (0.27-2.56)	1.89 (0.53, 6.72)
Tocilizumab vs abata	cept						
Analysis 1	Tocilizumab	6,369	<11	7,031	1.1	1.42 (0.68-2.62)	
	Abatacept	6,369	17	7,492	1.2	2.27 (1.32-3.63)	0.65 (0.30, 1.41)
Analysis 2	Tocilizumab	3,949	29	7,953	2.0	3.65 (2.44-5.24)	
	Abatacept	3,949	20	7,960	2.0	2.51 (1.53-3.88)	1.45 (0.82, 2.57)
Analysis 3	Tocilizumab	3,494	<11	4,568	1.3	2.19 (1.05-4.02)	
	Abatacept	3,494	<11	4,690	1.3	2.13 (1.02-3.92)	1.03 (0.43-2.48)
Analysis 4	Tocilizumab	6,369	<11	7,034	1.1	1.00 (0.40-2.05)	
	Abatacept	6,369	<11	7,500	1.2	1.20 (0.55-2.28)	0.86 (0.32, 2.32)
TNFi vs abatacept							
Analysis 1	TNFi	11,976	27	15,427	1.3	1.75 (1.15-2.55)	
	Abatacept	11,976	36	16,243	1.3	2.22 (1.55-3.07)	0.79 (0.48, 1.31)
Analysis 2	TNFi	7,940	71	17,591	2.2	4.04 (3.15-5.09)	
	Abatacept	7,940	63	17,632	2.2	3.57 (2.75-4.57)	1.13 (0.80, 1.59)
Analysis 3	TNFi	7127	21	11,304	1.6	1.86 (1.14-2.84)	
	Abatacept	7127	28	11,592	1.6	2.41 (1.60-3.49)	0.78 (0.44-1.37)
Analysis 4	TNFi	11,976	20	15,432	1.3	1.30 (0.79-2.00)	
	Abatacept	11,976	19	16,263	1.4	1.17 (0.70-1.82)	1.12 (0.60, 2.09)

^{*}Analysis 1: 'As-treated' follow-up approach; Analysis 2: 'As-started' follow-up approach incorporating a 6-month induction period; Analysis 3: Incorporating a 6-month 'symptom to diagnosis' period' and Analysis 4: Alternate outcome definition (See Methods for additional description of analytic approach).
† Numbers <11 are suppressed according to Data Use Agreement with the Centers for Medicare and Medicare Services