Supplementary Material

Supplementary Table 1. Search Strategy.

Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® <1946-Present>	
#	**Searches**
1	Antirheumatic Agents/
2	(anti rheumatic* or antirheumatic* or DMARD*).tw,kf.
3	Methotrexate/
4	(methotrexate or amethopterin or mexate or 3ig1e710zn or yl5fz2y5u1 or rheumatrex or trexall).tw,kf,rn.
5	Hydroxychloroquine/
6	(Hydroxychloroquine or 4qwg6n8qkh or 8q2869cnvh or hydroxychlorochin or oxychlorochin or oxychloroquine or plaquenil or quinoric or doloquine).tw,kf,rn.
7	Sulfasalazine/
8	(Sulfasalazin* or asulfidine or azulfadine or azulfidine or pyralin or pleon or salazopyrin or salazosulfapyridine or salicylazosulfapyridine or sulphasalazin* or ucine or ulcol or 3xc8guz6cb or sulfazine).tw,kf,rn.
9	Leflunomide/
10	(75706-12-6 or leflunomid* or arava or arabloc or g162gk9u4w or hwa 486).tw,kf,rn.
11	Tumor Necrosis Factor-alpha/
12	(tumo?r necrosis factor* or cachectin or TNF).tw,kf.
13	Etanercept/
14	(185243-69-0 or enbrel or erelzi or etanercept or op401g7ojc or tnfr-fc).tw,kf,rn.
15	Adalimumab/
16	(adalimumab* or amievita or cyltezo or d2e7 anibod* or fys6t7f842 or humira).tw,kf,rn.
17	Infliximab/
18	(Infliximab or 170277-31-3 or b72hh48flu or inflectra or remicade or renflexis).tw,kf,rn.
19	(Golimumab or simponi or CNTO-148).tw,kf,rn.
20	Certolizumab Pegol/
21	(Certolizumab or 428863-50-7 or cdp 870 or cimzia or umd07x179e).tw,kf,rn.
22	Rituximab/
23	(rituximab or 174722-31-7 or 4f4x42syq6 or gp2013 or idec c2b8 or mabthera or rituxan).tw,kf,rn.
24	Abatacept/
25	(abatacept or 332348-12-6 or 7d0yb67s97 or bms 188667 or bms 224818 or belatacept or lea29y or nulojix or orencia).tw,kf,rn.
26	Interleukin-6/
27	(interleukin 6 or beta 2 inferon* or IL6 or IL 6).tw,kf.
28	((b cell differentiation* or b cell stimulat* or hepatocyte stimulat*) adj3 factor*).tw,kf.
29	(growth factor* adj3 (hybridoma or plasmacytoma)).tw,kf.
30	(myeloid adj3 inducing protein*).tw,kf.
31	(tocilizumab or actemra or RoActemra or Atlizumab).tw,kf.
32	(sarilumab or kevzara).tw,kf.

33	Janus Kinase Inhibitors/
34	((janus kinase or JAK) adj3 inhibit*).tw,kf.
35	(tofacitinib or Xeljanz or Jaquinus or Tofacinix).tw,kf.
36	(baricitinib or Olumiant).tw,kf.
37	(upadacitinib or Rinvoq or ABT-494).tw,kf.
38	((T cell or Tcell) adj2 costimulatory adj3 inhibit*).tw,kf.
39	or/1-38
40	dementia/ or alzheimer disease/ or dementia, vascular/ or frontotemporal dementia/ or lewy body disease/ or "Pick Disease of the Brain"/
41	(dementia* or amentia* or alzheimer* or ADRD).tw,kf.
42	((disease* or disorder* or illness*) adj3 (pick* or wilhelmsen lynch or lewy bod*)).tw,kf.
43	(binswanger adj3 (disease* or encephalopath*)).tw,kf.
44	(subcortical adj3 (encephalopath* or leukoencephalopath*)).tw,kf.
45	((brain* or lobar*) adj2 atroph*).tw,kf.
46	(neuron* cytoplasmic inclusion* or CADASIL).tw,kf.
47	or/40-46
48	39 and 47
49	animals/ not (humans/ or human*.mp. or patient*.mp. or people*.mp. or person*.mp.)
50	48 not 49
Embase Classic+Embase <1947 to 2023 October 25>	
1	antirheumatic agent/
2	(anti rheumatic* or antirheumatic* or DMARD*).tw,kf.
3	disease modifying antirheumatic drug/
4	methotrexate/
5	(methotrexate or amethopterin or mexate or 3ig1e710zn or yl5fz2y5u1 or rheumatrex or trexall or abitextrate or metatrexan or antifolan or brimexate or emt?exat* or folex or methoblastin or metoject or metrotex or nordimet or novatrex or rasuvo or reditrex or tremetex or trexeron or xatmep or zlatal or zexate or Methylaminopterin or Maxtrex).tw,kf,du,dy,tn.
6	hydroxychloroquine/
7	(Hydroxychloroquine or 4qwg6n8qkh or 8q2869cnvh or hydroxychlorochin or oxychlorochin or oxychloroquine or plaquenil or quinoric or doloquine or hydroc?loroquine or quensyl).tw,kf,du,dy,tn.
8	salazosulfapyridine/
9	(Sulf?salazin* or asulfidine or azulfadine or azulfidine or pyralin or pleon or colopleon or salazopyrin* or salazosulfapyridine or salicylazosulfapyridine or sulphasalazin* or ucine or ulcol or 3xc8guz6cb or sulfazine or azopyrin* or azosulfid* or benzosulfa).tw,kf,du,dy,tn.
10	leflunomide/
11	(75706-12-6 or leflunomid* or arava or arabloc or g162gk9u4w or hwa 486 or respo).tw,kf,du,dy,tn.
12	tumor necrosis factor/
13	(tumo?r necrosis factor* or cachectin or TNF).tw,kf.
14	etanercept/

15	(185243-69-0 or e?brel or erelzi or etanercept or op401g7ojc or tnfr-fc or altebrel or avent or benepali or brenzys or davictrel or enerceptan).tw,kf,dy,du,tn.
16	adalimumab/
17	(adalimumab* or amievita or cyltezo or d2e7 anibod* or fys6t7f842 or humira or abrilada or adaly).tw,kf,dy,du,tn.
18	infliximab/
19	(Infliximab or 170277-31-3 or b72hh48flu or inflectra or remicade or renflexis or remsima or revellex or zessly or ixifi).tw,kf,du,dy,tn.
20	golimumab/
21	(Golimumab or simponi or CNTO-148 or shinponi).tw,kf,du,dy,tn.
22	certolizumab pegol/
23	(Certolizumab or 428863-50-7 or cdp 870 or cimzia or umd07x179e or simziya or xcimzane).tw,kf,dy,du,tn.
24	rituximab/
25	(rituximab or 174722-31-7 or 4f4x42syq6 or gp2013 or idec c2b8 or mabthera or rituxan or acellbia or blitzima or cimabior or halpryza or kikuzubam or mabthera or red?itux or retuxira or riabni or ristova or ritemvia or ritucad or ritumax or rituximab or rituxin or rituzena or rixathon or riximyo or ruxience or tidecron or truxima or tuxella or zytux).tw,kf,dy,du,tn.
26	abatacept/
27	(abatacept or 332348-12-6 or 7d0yb67s97 or bms 188667 or bms 224818 or belatacept or lea29y or nulojix or orencia).tw,kf,dy,du,tn.
28	interleukin 6/
29	(interleukin 6 or IL6 or IL 6 or interleukin b or interleukin hp1).tw,kf.
30	((b cell differentiation* or b cell stimulat* or hepatocyte stimulat*) adj3 factor*).tw,kf.
31	(growth factor* adj3 (hybridoma or plasmacytoma)).tw,kf.
32	(myeloid adj3 inducing protein*).tw,kf.
33	tocilizumab/
34	(tocilizumab or actemra or RoActemra or Atlizumab or lusinex or roactemra).tw,kf,dy,du,tn.
35	sarilumab/
36	(sarilumab or kevzara).tw,kf,dy,du,tn.
37	Janus kinase inhibitor/
38	((janus kinase or JAK) adj3 inhibit*).tw,kf.
39	tofacitinib/
40	(tofacitinib or Xeljanz or Jaquinus or Tofacinix or tasocitinib).tw,kf,du,dy,tn.
41	baricitinib/
42	(baricitinib or Olumiant).tw,kf,dy,du,tn.
43	upadacitinib/
44	(upadacitinib or Rinvoq or ABT-494).tw,kf,dy,du,tn.
45	((T cell or Tcell) adj2 costimulatory adj3 inhibit*).tw,kf.
46	or/1-45
47	dementia/
48	Alzheimer disease/
49	multiinfarct dementia/

50	frontotemporal dementia/
51	diffuse Lewy body disease/
52	Pick presenile dementia/
53	dementia/ or binswanger encephalopathy/ or cadasil/ or mixed dementia/ or presenile dementia/ or senile dementia/
54	(dementia* or amentia* or alzheimer* or ADRD).tw,kf.
55	((disease* or disorder* or illness*) adj3 (pick* or wilhelmsen lynch or lewy bod*)).tw,kf.
56	(binswanger adj3 (disease* or encephalopath*)).tw,kf.
57	(subcortical adj3 (encephalopath* or leukoencephalopath*)).tw,kf.
58	((brain* or lobar*) adj2 (degenerat* or atroph*)).tw,kf.
59	(neuron* cytoplasmic inclusion* or CADASIL).tw,kf.
60	(major adj3 neurocognitive disorder*).tw,kf.
61	or/47-60
62	46 and 61
63	(exp animal/ or exp invertebrate/ or nonhuman/ or animal experiment/ or animal tissue/ or animal model/ or exp plant/ or exp fungus/) not (exp human/ or human tissue/)
64	62 not 63
APA PsycInfo <1806 to October Week 3 2023>	
1	(anti rheumatic* or antirheumatic* or DMARD*).tw.
2	(methotrexate or amethopterin or mexate or 3ig1e710zn or yl5fz2y5u1 or rheumatrex or trexall or abitextrate or metatrexan or antifolan or brimexate or emt?exat* or folex or methoblastin or metoject or metrotex or nordimet or novatrex or rasuvo or reditrex or tremetex or trexeron or xatmep or zlatal or zexate or Methylaminopterin or Maxtrex).tw.
3	(Hydroxychloroquine or 4qwg6n8qkh or 8q2869cnvh or hydroxychlorochin or oxychlorochin or oxychloroquine or plaquenil or quinoric or doloquine or hydroc?loroquine or quensyl).tw.
4	(Sulf?salazin* or asulfidine or azulfadine or azulfidine or pyralin or pleon or colopleon or salazopyrin* or salazosulfapyridine or salicylazosulfapyridine or sulphasalazin* or ucine or ulcol or 3xc8guz6cb or sulfazine or azopyrin* or azosulfid* or benzosulfa).tw.
5	(75706-12-6 or leflunomid* or arava or arabloc or g162gk9u4w or hwa 486 or respo).tw.
6	tumor necrosis factor/
7	(tumo?r necrosis factor* or cachectin or TNF).tw.
8	(185243-69-0 or e?brel or erelzi or etanercept or op401g7ojc or tnfr-fc or altebrel or avent or benepali or brenzys or davictrel or enerceptan).tw.
9	(adalimumab* or amievita or cyltezo or d2e7 anibod* or fys6t7f842 or humira or abrilada or adaly).tw.
10	(Infliximab or 170277-31-3 or b72hh48flu or inflectra or remicade or renflexis or remsima or revellex or zessly or ixifi).tw.
11	(Golimumab or simponi or CNTO-148 or shinponi).tw.
12	(Certolizumab or 428863-50-7 or cdp 870 or cimzia or umd07x179e or simziya or xcimzane).tw.

13	(rituximab or 174722-31-7 or 4f4x42syq6 or gp2013 or idec c2b8 or mabthera or rituxan or acellbia or blitzima or cimabior or halpryza or kikuzubam or mabthera or red?itux or retuxira or riabni or ristova or ritemvia or ritucad or ritumax or rituximab or rituxin or rituzena or rixathon or riximyo or ruxience or tidecron or truxima or tuxella or zytux).tw.
14	(abatacept or 332348-12-6 or 7d0yb67s97 or bms 188667 or bms 224818 or belatacept or lea29y or nulojix or orencia).tw.
15	interleukins/
16	(interleukin 6 or IL6 or IL 6 or interleukin b or interleukin hp1).tw.
17	((b cell differentiation* or b cell stimulat* or hepatocyte stimulat*) adj3 factor*).tw.
18	(growth factor* adj3 (hybridoma or plasmacytoma)).tw.
19	(myeloid adj3 inducing protein*).tw.
20	(tocilizumab or actemra or RoActemra or Atlizumab or lusinex or roactemra).tw.
21	(sarilumab or kevzara).tw.
22	((janus kinase or JAK) adj3 inhibit*).tw.
23	(tofacitinib or Xeljanz or Jaquinus or Tofacinix or tasocitinib).tw.
24	(baricitinib or Olumiant).tw.
25	(upadacitinib or Rinvoq or ABT-494).tw.
26	((T cell or Tcell) adj2 costimulatory adj3 inhibit*).tw.
27	or/1-26
28	dementia/ or alzheimer's disease/ or dementia with lewy bodies/ or frontotemporal lobar degeneration/ or presenile dementia/ or senile dementia/ or vascular dementia/ or picks disease/
29	semantic dementia/
30	(dementia* or amentia* or alzheimer* or ADRD).tw.
31	((disease* or disorder* or illness*) adj3 (pick* or wilhelmsen lynch or lewy bod*)).tw.
32	(binswanger adj3 (disease* or encephalopath*)).tw.
33	(subcortical adj3 (encephalopath* or leukoencephalopath*)).tw.
34	((brain* or lobar*) adj2 (degenerat* or atroph*)).tw.
35	(neuron* cytoplasmic inclusion* or CADASIL).tw.
36	(major adj3 neurocognitive disorder*).tw.
37	or/28-36
38	27 and 37
Wiley Cochrane	
#1	[mh ^"Antirheumatic Agents"]
#2	(anti rheumatic* or antirheumatic* or DMARD*):ti,ab,kw
#3	[mh ^Methotrexate]
#4	(methotrexate or amethopterin or mexate or 3ig1e710zn or yl5fz2y5u1 or rheumatrex or trexall or abitextrate or metatrexan or antifolan or brimexate or emt?exat* or folex or methoblastin or metoject or metrotex or nordimet or novatrex or rasuvo or reditrex or tremetex or trexeron or xatmep or zlatal or zexate or Methylaminopterin or Maxtrex):ti,ab,kw
#5	[mh ^Hydroxychloroquine]

#6	(Hydroxychloroquine or 4qwg6n8qkh or 8q2869cnvh or hydroxychlorochin or oxychlorochin or oxychloroquine or plaquenil or quinoric or doloquine or hydroc?loroquine or quensyl):ti,ab,kw
#7	[mh ^Sulfasalazine]
#8	(Sulf?salazin* or asulfidine or azulfadine or azulfidine or pyralin or pleon or salazopyrin or salazosulfapyridine or salicylazosulfapyridine or sulphasalazin* or ucine or ulcol or 3xc8guz6cb or sulfazine or azopyrin* or azosulfid* or benzosulfa):ti,ab,kw
#9	[mh ^Leflunomide]
#10	(75706 12 6 or leflunomid* or arava or arabloc or g162gk9u4w or hwa 486 or respo):ti,ab,kw
#11	[mh ^"Tumor Necrosis Factor-alpha"]
#12	(tumo?r necrosis factor* or cachectin or TNF):ti,ab,kw
#13	[mh ^Etanercept]
#14	(185243 69 0 or e?brel or erelzi or etanercept or op401g7ojc or tnfr-fc or altebrel or avent or benepali or brenzys or davictrel or enerceptan):ti,ab,kw
#15	[mh ^Adalimumab]
#16	(adalimumab* or amievita or cyltezo or d2e7 anibod* or fys6t7f842 or humira or abrilada or adaly):ti,ab,kw
#17	[mh ^Infliximab]
#18	(Infliximab or 170277 31 3 or b72hh48flu or inflectra or remicade or renflexis or remsima or revellex or zessly or ixifi):ti,ab,kw
#19	(Golimumab or simponi or CNTO-148 shinponi):ti,ab,kw
#20	[mh ^"Certolizumab Pegol"]
#21	(Certolizumab or 428863 50 7 or cdp 870 or cimzia or umd07x179e or simziya or xcimzane):ti,ab,kw
#22	[mh ^Rituximab]
#23	(rituximab or 174722 31 7 or 4f4x42syq6 or gp2013 or idec c2b8 or mabthera or rituxan or acellbia or blitzima or cimabior or halpryza or kikuzubam or mabthera or red?itux or retuxira or riabni or ristova or ritemvia or ritucad or ritumax or rituximab or rituxin or rituzena or rixathon or riximyo or ruxience or tidecron or truxima or tuxella or zytux):ti,ab,kw
#24	[mh ^Abatacept]
#25	(abatacept or 332348 12 6 or 7d0yb67s97 or bms 188667 or bms 224818 or belatacept or lea29y or nulojix or orencia):ti,ab,kw
#26	[mh ^"Interleukin-6"]
#27	(interleukin 6 or IL6 or IL 6 or interleukin b or interleukin hp1):ti,ab,kw
#28	((b cell differentiation* or b cell stimulat* or hepatocyte stimulat*) NEAR/3 factor*):ti,ab,kw
#29	(growth factor* NEAR/3 (hybridoma or plasmacytoma)):ti,ab,kw
#30	(myeloid NEAR/3 inducing protein*):ti,ab,kw
#31	(tocilizumab or actemra or RoActemra or Atlizumab or lusinex or roactemra):ti,ab,kw
#32	(sarilumab or kevzara):ti,ab,kw
#33	[mh ^"Janus Kinase Inhibitors"]
#34	((janus kinase or JAK) NEAR/3 inhibit*):ti,ab,kw
#35	(tofacitinib or Xeljanz or Jaquinus or Tofacinix or tasocitinib):ti,ab,kw

#36	(baricitinib or Olumiant):ti,ab,kw
#37	(upadacitinib or Rinvoq or ABT-494):ti,ab,kw
#38	((T cell or Tcell) NEAR/2 costimulatory NEAR/3 inhibit*):ti,ab,kw
#39	{or #1-#38}
#40	[mh ^dementia] or [mh ^"alzheimer disease"] or [mh ^"dementia, vascular"] or [mh ^"frontotemporal dementia"] or [mh ^"lewy body disease"] or [mh ^"Pick Disease of the Brain"] or [mh ^"mixed dementias"
#41	(dementia* or amentia* or alzheimer* or ADRD):ti,ab,kw
#42	((disease* or disorder* or illness*) NEAR/3 (pick* or wilhelmsen lynch or lewy bod*)):ti,ab,kw
#43	(binswanger NEAR/3 (disease* or encephalopath*)):ti,ab,kw
#44	(subcortical NEAR/3 (encephalopath* or leukoencephalopath*)):ti,ab,kw
#45	((brain* or lobar*) NEAR/2 (degenerat* or atroph*)):ti,ab,kw
#46	(neuron* cytoplasmic inclusion* or CADASIL):ti,ab,kw
#47	(major NEAR/3 neurocognitive disorder*):ti,ab,kw
#48	{or #40-#47}
#49	#39 AND #48

Supplementary Table 2. Definitions of Important Biases.

	Description
Confounding by Indication	Confounding by indication results from between-group differences in risk factors that could have influenced who was given which treatment. When the comparator group is not properly chosen (e.g. first-line vs. second-line therapies or users vs. non-users in many instances), substantial confounding is often expected[1–3].
Selection Bias	Selection bias is a category of biases due to systematic errors in participant selection. Studies using the entire exposure data during follow-up to determine the cohort entry are prone to selection bias[4].
Immortal Time Bias	Immortal time bias occurs when at-risk time prior to drug initiation is misclassified into the exposed or excluded from the analysis[5,6]. If the follow-up time of the exposed and unexposed starts from cohort entry, then bias due to misclassified immortal time could be introduced, and this source of bias will dramatically overestimate the benefit. If the follow-up time of the exposed starts from drug initiation (i.e., immortal time was excluded), the degree of overestimation will be smaller, but substantial bias may still exist. A common cause of immortal time bias is the use of the entire follow-up data to define baseline exposures. Immortal time bias can be eliminated with appropriate methodology such as an active-comparator new-user cohort design (when properly conducted) and time-varying exposure definition[2,6].
Time-Window Bias	The available lookback windows for exposure assessment are not balanced in length between outcome groups, such that the cases are more likely to have the exposure than the controls (or vice versa)[7].
Reverse Causality	Early symptoms of signs prior to actual dementia diagnosis may influence the decision to initiation or discontinue treatments. When the treatment group is more likely to be prescribed to individuals with early dementia symptoms (or vice versa), the estimate will be biased[8]. Lag time is a common approach to mitigate the potential for reverse causality[9].
Prevalent-User Bias	Prevalent-user bias can be introduced if the follow-up starts after the time of drug initiation[10,11]. In the presence of prevalent-user bias, events occurring early after drug initiation could be missed, at-risk time could not be properly calculated, and confounding could not be adjusted based on pre-exposure data. Also, selection towards less vulnerable individuals could also be a concern.
Overadjustment Bias	Bias resulting from adjusting post-exposure covariates. When covariates are defined partially or entirely based on data after drug

	initiation, mediators may be adjusted, which distorts the association between the exposure and outcome. To properly estimate the association between the exposure and outcome, covariates should be defined based on pre-exposure data[12].

Supplementary Table 3. Study Characteristics.

Study	Data source	Population characteristics	Exposure ascertainment method	Outcome definition	Population age (years)	Female proportions	Study period
Chou 2017	Taiwan's National Health Insurance Research Database	People with rheumatoid arthritis aged ≥ 20	Health insurance claims	A diagnosis of dementia based on ICD-9 codes (290, 294.1, and 331.0)	Mean = 74.2	78.3%	2000-2011
Chou 2016	Verisk Health claims database	People with rheumatoid arthritis aged ≥ 18	Health insurance claims	Alzheimer's Disease diagnosis based on ICD-9 codes	Mean = 75.5	75.6%	2000-2007
Desai 2022	Medicare	People with rheumatoid arthritis aged ≥ 65	Health insurance claims	Alzheimer's disease and related dementia based on inpatient and outpatient claims	Mean = 72.2	82.2%	2007-2017
Fardet 2019	The Health Improvement Network	People with connective tissue diseases and 68% were diagnosed with rheumatoid arthritis	Primary care prescription records	A medical record of Alzheimer's disease or vascular dementia	Median = 56	77.7%	1990-2016
Huang 2019	National Health Insurance Research Database	People with rheumatoid arthritis aged ≥ 20	Health insurance claims	2 outpatient claims or 1 inpatient claim with dementia diagnosis	Unknown	Unknown	2000-2005
Judge 2017	UK Clinical Practice Research Datalink	People newly diagnosed with rheumatoid arthritis	Primary care prescription records	Read codes of dementia	Mean = 61.9	70.6%	1995-2011
Kern 2021	Optum & Marketscan	People with rheumatoid arthritis aged ≥ 18	Health insurance claims	Two diagnoses of dementia in one year	Mean = 55 (Optum); Mean = 73 (Marketscan)	75.7% (Optum); 71.9% (Marketscan)	2000-2019
Kodishala 2023	Rochester Epidemiology Project	People with rheumatoid rheumatoid arthritis aged ≥ 50	Chart review	2 records of dementia diganoses at least 30 days apart	Mean = 65.1	65.2%	1980-2014

Newby 2020	European Medical Information Framework	People with rheumatoid arthritis aged ≥ 50 in the UK, Spain, Denmark, and the Netherlands	Electronic health records	The presence of a first-ever clinical or referral record of dementia	Mean = 79.6	87.0%	1995-2016
Sattui 2021	Medicare	People with rheumatoid arthritis aged ≥ 65 years	Health insurance claims	1 inpatient diagnosis, 2 outpatient diagnoses, or 1 prescription of dementia-specific medication	Median = 74	81.3%	2006-2014
Sattui 2022	Medicare & Medicaid	People with rheumatoid arthritis aged ≥ 40 years	Health insurance claims	1 inpatient diagnosis, 2 outpatient diagnoses, or 1 prescription of dementia-specific medication	Mean ~ 65-74	81.0%	2006-2017
Varma 2023	Medicare	People with rheumatoid arthritis aged ≥ 65 years without prior use of any disease modifying antirheumatic treatments	Health insurance claims	Alzheimer's disease and related dementia based on inpatient and outpatient claims	Mean = 73.8	76.2%	2007-2017
Zheng 2022	US Department of Veterans Affairs Corporate Data Warehouse	People with rheumatoid arthritis	Pharmacy data	Two diagnostic codes for dementia in 12 months	Mean = 66.1	13.8%	2000-2020
Zhou 2020	IBM Watson Health Explorys Cohort Discovery platform	People with rheumatoid arthritis and a prescription for rheumatoid arthritis aged ≥ 18	Health insurance claims	A diagnosis code for Alzheimer's disease	Unknown	Unknown	Unknown

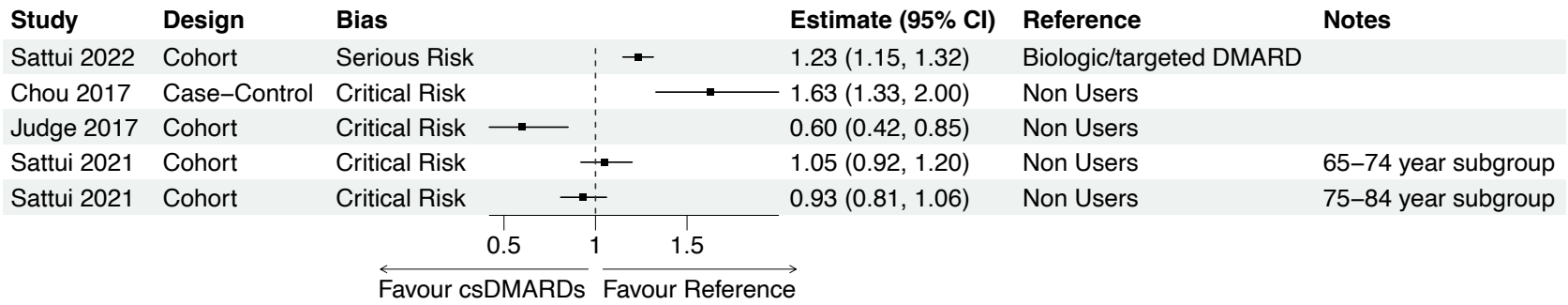
Supplementary Table 4. Common Sources of Bias in Pharmacoepidemiologic Studies for Dementia.

Study	Immortal Time Bias	Time-Window Bias	Reverse Causality	Prevalent-user bias	Overadjustment Bias
Chou 2017	NA	Critical Risk	Serious Risk	NA	Serious Risk
Chou 2016	NA	Low Risk	Moderate Risk	NA	Critical Risk
Desai 2022	Low Risk	NA	Low Risk	Low Risk	Low Risk
Fardet 2019	Moderate Risk	NA	Serious Risk	Serious Risk	No Info
Huang 2019	Critical Risk	NA	Serious Risk	Moderate Risk	Critical Risk
Judge 2017	Moderate Risk	NA	Serious Risk	Moderate Risk	Low Risk
Kern 2021	Low Risk	NA	Serious Risk	Low Risk	Low Risk
Kodishala 2023	Low Risk	NA	Serious Risk	Moderate Risk	Serious Risk
Newby 2020	NA	Critical Risk	Serious Risk	NA	Serious Risk
Sattui 2021	Low Risk	NA	Serious Risk	Critical Risk	Low Risk
Sattui 2022	Low Risk	NA	Moderate Risk	Low Risk	Low Risk
Varma 2023	Low Risk	NA	Low Risk	Low Risk	Low Risk
Zheng 2022	Moderate Risk	NA	Serious Risk	Moderate Risk	Low Risk
Zhou 2020	NA	Critical Risk	Serious Risk	NA	Moderate Risk

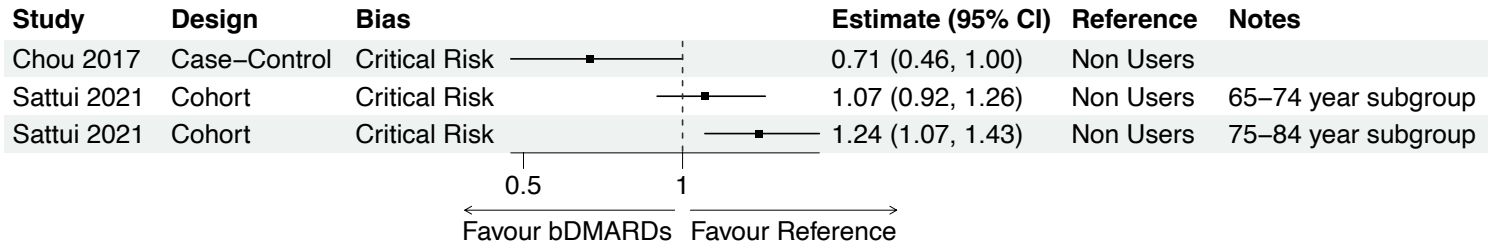
Supplementary Table 5. Certainty of Evidence.

Study	Indirectness [a] (0-2)	Imprecision (0-1)	Risk of Bias (0-3)	Publication Bias (0-1)	Plausible Residual Confounding (0-1)	Certainty Score
Chou 2017	Serious	Substantial	Critical Risk	Minimal	Substantial	1
Chou 2016	Serious	Substantial	Critical Risk	Minimal	Substantial	1
Desai 2022 (for tofacitinib and tocilizumab)	Minimal	Substantial	Low Risk	Minimal	Minimal	7
Desai 2022 (for TNF inhibitors)	Minimal	Minimal	Low Risk	Minimal	Minimal	8
Fardet 2019	Serious	Substantial	Serious Risk	Minimal	Substantial	2
Huang 2019	Serious	Minimal	Critical Risk	Minimal	Substantial	2
Judge 2017	Serious	Minimal	Critical Risk	Minimal	Substantial	2
Kern 2021	Moderate	Substantial	Moderate Risk	Minimal	Minimal	5
Kodishala 2023	Serious	Substantial	Critical Risk	Minimal	Substantial	1
Newby 2020	Serious	Substantial	Critical Risk	Minimal	Substantial	1
Sattui 2021	Serious	Minimal	Critical Risk	Minimal	Substantial	2
Sattui 2022	Moderate	Minimal	Serious Risk	Minimal	Substantial	4
Varma 2023	Minimal	Minimal	Low Risk	Minimal	Minimal	8
Zheng 2022	Serious	Minimal	Critical Risk	Minimal	Substantial	2
Zhou 2020	Serious	Minimal	Critical Risk	Minimal	Substantial	2

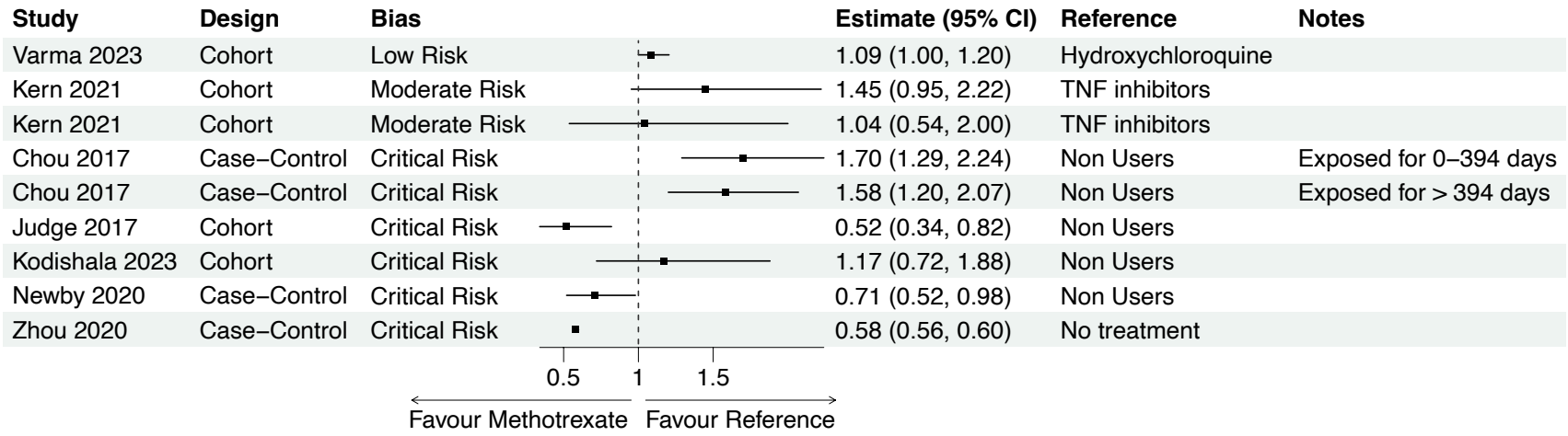
a. Evidence is considered “direct” (or “minimally indirect”) when the study directly compares outcomes important to patients between interventions in a clinically relevant population[13]. Indirect evidence could result from surrogate outcomes, non-use or no treatment as a comparator, a comparator from a different clinical setting, and over-restriction of study eligibility. In the present systematic review, studies comparing one drug to an active comparator positioned similarly in clinical practice (e.g. hydroxychloroquine vs. methotrexate as first-line therapies) in a broad population of rheumatoid arthritis are considered to have minimal indirectness.



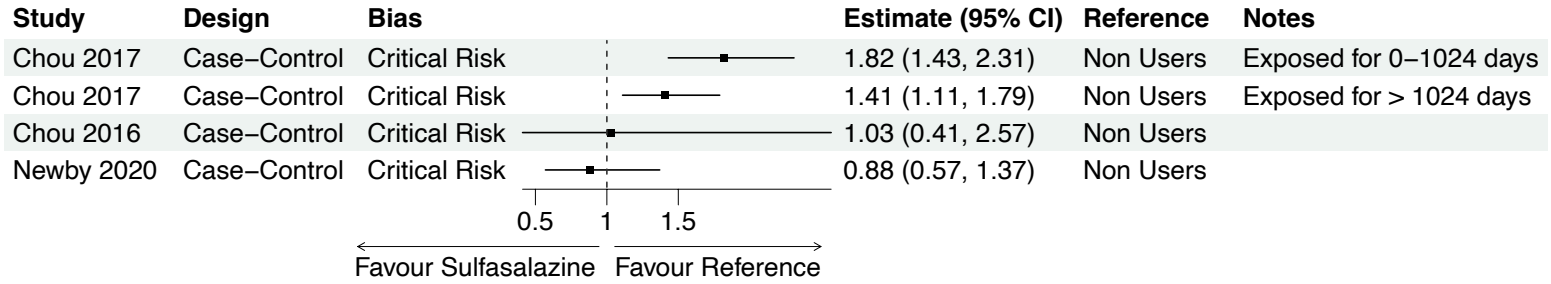
Supplementary Figure 1. Forest Plot of Studies Examining Conventional Synthetic DMARDs (csDMARDs).



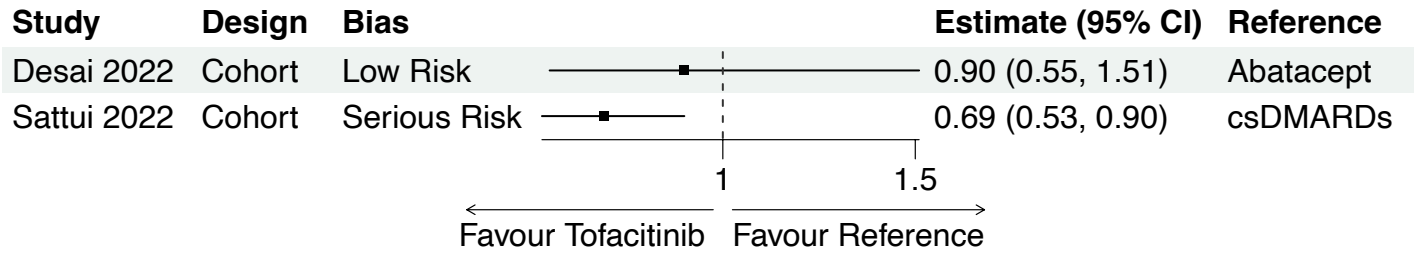
Supplementary Figure 2. Forest Plot of Studies Examining Biologic DMARDs (bDMARDs).



Supplementary Figure 3. Forest Plot of Studies Examining Methotrexate.



Supplementary Figure 4. Forest Plot of Studies Examining Sulfasalazine.



Supplementary Figure 5. Forest Plot of Studies Examining Tofacitinib.

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