Online supplement to Benefits of Methotrexate Use on Cardiovascular Disease Risk Among Rheumatoid Arthritis Patients Initiating Biologic Disease-modifying Antirheumatic Drugs. *The Journal of Rheumatology.*doi:10.3899/jrheum.191326

ONLINE SUPPLEMENTARY MATERIAL

Supplementary Table 1. Incidence rates and hazard ratios for composite CVD events associated with time varying methotrexate use, by specific biologic DMARD

		Methotrexate† unexposed			Methotrexate† exposed			Contrast‡
	Biologic DMARDS	Event	Person years	Incidence rate (95% CI)	Event	Person years	Incidence rate (95% CI)	
Myocardial infarction or stroke or fatal CVD	Abatacept	317	18237	17·4 (15·6, 19·4)	102	8909	11·4 (9·4, 13·9)	0·74 (0·59, 0·93)
	Adalimumab	161	9852	16·3 (14·0, 19·1)	81	6130	13·2 (10·6, 16·4)	0·91 (0·69, 1·20)
	Certolizumab	70	3819	18·3 (14·5, 23·2)	20	2152	9·3 (6·0, 14·4)	0·59 (0·36, 0·98)
	Etanercept	163	11189	14·6 (12·5, 17·0)	74	6042	12·2 (9·8, 15·4)	0·93 (0·70, 1·23)
	Golimumab	54	2646	20·4 (15·6, 26·6)	16	1503	10·6 (6·5, 17·4)	0·59 (0·34, 1·04)
	Infliximab	334	14891	22·4 (20·1, 25·0)	180	14060	12·8 (11·1, 14·8)	0·64 (0·54, 0·78)
	Rituximab	140	7660	18·3 (15·5, 21·6)	45	3302	13·6 (10·2, 18·3)	0·91 (0·65, 1·29)
	Tocilizumab	85	5834	14·6 (11·8, 18·0)	19	2214	8·6 (5·5, 13·5)	0·68 (0·41, 1·12)
Myocardial infarction	Abatacept	166	18,327	9·1 (7·8, 10·6)	52	8,944	5·8 (4·4, 7·6)	0·72 (0·51, 1·00)
	Adalimumab	79	9,900	8·0 (6·4, 10·0)	43	6,147	7·0 (5·2, 9·4)	1·00 (0·68, 1·46)
	Certolizumab	33	3,833	8·6 (6·1, 12·1)	13	2,157	6·0 (3·5, 10·4)	0·82 (0·43, 1·58)
	Etanercept	85	11,238	7·6 (6·1, 9·4)	40	6,056	6·6 (4·9, 9·0)	0·97 (0·66, 1·43)
	Golimumab	19	2,659	7·1 (4·6, 11·2)	<11	redacted	6·0 (3·1, 11·5)	0·95 (0·43, 2·10)
	Infliximab	198	15,010	13·2 (11·5, 15·2)	94	14,153	6·6 (5·4, 8·1)	0·57 (0·44, 0·73)
	Rituximab	69	7,704	9·0 (7·1, 11·3)	27	3,314	8·2 (5·6, 11·9)	1·13 (0·71, 1·77)
	Tocilizumab	45	5,854	7·7 (5·7, 10·3)	11	2,221	5·0 (2·7, 9·0)	0·74 (0·38, 1·45)
Stroke	Abatacept	155	18,413	8·4 (7·2, 9·9)	45	8,960	5·0 (3·8, 6·7)	0·66 (0·46, 0·92)
	Adalimumab	71	9,919	7·2 (5·7, 9·0)	31	6,155	5·0 (3·5, 7·2)	0·77 (0·50, 1·18)
	Certolizumab	31	3,833	8·1 (5·7, 11·5)	<11	redacted	3·7 (1·9, 7·4)	0·52 (0·24, 1·14)
	Etanercept	68	11,262	6·0 (4·8, 7·7)	31	6,065	5·1 (3·6, 7·3)	0·90 (0·59, 1·39)
	Golimumab	33	2,658	12·4 (8·8, 17·5)	<11	1,505	4·7 (2·2, 9·8)	0·42 (0·18, 0·95)
	Infliximab	136	15,069	9·0 (7.6, 10.7)	89	14,164	6·3 (5·1, 7·7)	0·77 (0·58, 1·01)
	Rituximab	65	7,715	8·4 (6·6, 10·7)	18	3,321	5·4 (3·4, 8·6)	0·76 (0·45, 1·29)
	Tocilizumab	40	5,864	6·8 (5·0, 9·3)	<11	redacted	4·5 (2·4, 8·4)	0·74 (0·37, 1·48)
Myocardial infarction	Abatacept	304	18,237	16·7 (14·9, 18·7)	95	8,909	10·7 (8·7, 13·0)	0·72 (0·56, 0·91)
	Adalimumab	148	9,852	15·0 (12·8, 17·7)	74	6,130	12·1 (9·6, 15·2)	0·90 (0·68, 1·20)

or stroke	Certolizumab	62	3,819	16·2 (12·7, 20·8)	20	2,152	9·3 (6·0, 14·4)	0·66 (0·40, 1·11)
	Etanercept	145	11,189	13·0 (11·0, 15·3)	70	6,042	11·6 (9·2, 14·6)	0·98 (0·73, 1·31)
	Golimumab	52	2,646	19·7 (15·0, 25·8)	15	1,503	10·0 (6·0, 16·6)	0·57 (0·32, 1·02)
	Infliximab	323	14,891	21·7 (19·5, 24·2)	175	14,060	12·5 (10·7, 14·4)	0·64 (0·53, 0·78)
	Rituximab	127	7,660	16·6 (13·9, 19·7)	45	3,302	13·6 (10·2, 18·3)	1·00 (0·71, 1·41)
	Tocilizumab	81	5,834	13·9 (11·2, 17·3)	19	2,214	8·6 (5·5, 13·5)	0·71 (0·43, 1·17)
Myocardial infarction, stroke , angina, PCI, CABG ,fatal CVD	Abatacept	260	13,825	18.8 (16.7, 21.2)	96	6,978	13.8 (11.3, 16.8)	0.76 (0.60, 0.98)
	Adalimumab	123	7,855	15.7 (13.1, 18.7)	69	5,033	13.7 (9.1, 20.7)	0.91 (0.68, 1.24)
	Certolizumab	53	2,889	18.3 (14.0, 24.0)	23	1,674	13.7 (9.1, 20.7)	0.798 (0.48, 1.31)
	Etanercept	129	8,868	14.5 (12.2, 17.3)	68	4,886	13.9 (11.0, 17.7)	0.98 (0.73, 1.33)
	Golimumab	38	2,025	18.8 (13.7, 25.8)	13	1,179	11.0 (6.4, 19.0)	0.61 (0.32, 1.15)
	Infliximab	263	11,660	22.6 (20.0, 25.5)	190	11,477	16.6 (14.4, 19.1)	0.76 (0.63, 0.93)
	Rituximab	110	5,672	19.4 (16.1, 23.4)	37	2,539	14.6 (10.6, 20.1)	0.83 (0.67, 1.21)
	Tocilizumab	60	4,465	13.4 (10.4, 17.3)	17	1,733	9.8 (6.1, 15.8)	0.77 (0.45, 1.33)

CI: Confidence interval; CVD: Cardiovascular disease; DMARDS: Disease-modifying antirheumatic drugs; HR: Hazard ratio; IR: Incidence rate per 1,000 person-years.
Redacted = data not shown to avoid disclosing cell sizes < 11
†Time varying methotrexate was defined as methotrexate day of supply with no extension.
‡In one model for each outcome, compares risk for time varying MTX versus nonuse within each biologic DMARD exposure row; adjusted for age, sex, race, Charlson comorbidity index, baseline MTX, hydroxychloroquine, leflunomide, sulfasalazine, heart failure, atrial fibrillation, abdominal aortic aneurism, peripheral arterial disease, diabetes, hyperlipidemia, hypertension, obesity, chronic kidney disease, chronic obstructive pulmonary disease, fibromyalgia, any hospitalized infection, any hospitalization, number of physician visit, time varying folic acid, nonsteroidal anti-inflammatory drug, statin potency, other lipid lowering drug use in baseline, number of biologic used prior initiation, oral steroid dose in six month before initiation, smoking, State Buy-In (poor), reasons other than age for eligible for Medicare, time varying folic acid, non-alcoholic fatty liver disease, and metabolic syndrome. Time varying folic acid was defined as days of supply with no extension. Time varying non-alcoholic fatty liver disease, and metabolic syndrome were defined using diagnosis code in both baseline and follow-up period.