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## COMPARATIVE RISK OF SERIOUS INFECTIONS AMONG REAL-WORLD USERS OF BIOLOGICS FOR PSORIASIS OR PSORIATIC ARTHRITIS

Short running title: Biologics-associated serious infections in PsO and PsA

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**Table S1.** National Drug Code (NDC), to define outpatient pharmacy dispensation claims, and Healthcare Common Procedure Coding System (HCPCS) codes, to define in-patient infusion.

<b>Class</b>	<b>Biologic</b>	<b>NDC code</b>	<b>HCPCS code</b>
IL-17	Ixekizumab	0002-1445	N/A
		0002-7724	
IL-17	Secukinumab	0078-0639	
IL-12/23	Ustekinumab	57894-054	J3357
		57894-060	J3358
		57894-061	C9487
			C9261
			C9989
TNF	Adalimumab	0074-0067	J0135
		0074-0124	
		0074-0243	
		0074-0554	
		0074-0616	
		0074-0817	
		0074-1539	
		0074-2540	
		0074-3799	
		0074-4339	
		0074-6347	
		0074-9374	
		50090-3530	
TNF	Certolizumab pegol	50474-700	J0717
		50474-710	
TNF	Etanercept	50090-3531	J1438
		58406-425	
		58406-435	
		58406-445	
		58406-446	
		58406-455	
		58406-456	
TNF	Golimumab	57894-070	J1602
		57894-071	
TNF	Infliximab	57894-030	J1745
		0069-0809	
		0006-4305	

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**Table S2.** Phototherapy, disease-modifying antirheumatic drug (DMARD) and nonsteroidal anti-inflammatory drug (NSAID) codes for covariate definition.

<b>Therapy</b>	<b>Description</b>	<b>Code type</b>	<b>Code</b>
Phototherapy	Photochemotherapy; psoralens and ultraviolet A (PUVA)	CPT	96912
Phototherapy	Photochemotherapy (Goeckerman and/or PUVA) for severe photoresponsive dermatoses requiring at least 4-hyphen8 hours of care under direct supervision of the physician (includes applications of medication and dressings)	CPT	96913
Phototherapy	Actinotherapy (ultraviolet light)	CPT	96900
Phototherapy	Photochemotherapy; tar and ultraviolet B (Goeckerman treatment) or petrolatum and ultraviolet B	CPT	96910
Phototherapy	Ultraviolet light therapy system panel, includes bulbs/lamps, timer and eye protection; treatment area 2 sq feet or less	CPT	E0691
Phototherapy	Ultraviolet light therapy system panel, includes bulbs/lamps, timer and eye protection; 4 ft panel	CPT	E0692
Phototherapy	Ultraviolet light therapy system panel, includes bulbs/lamps, timer and eye protection; 6 ft panel	CPT	E0693
Phototherapy	Ultraviolet multidirectional light therapy system in 6 ft cabinet, includes bulbs/lamps, timer and eye protection	CPT	E0694
DMARD	Methotrexate	NDC	
DMARD	Sulfasalazine	NDC	
DMARD	Leflunomide	NDC	
DMARD	Cyclosporine	NDC	
DMARD	Apremilast	NDC	
DMARD	Azathioprine	NDC	
DMARD	Retinoids	NDC	
NSAID	Celecoxib	NDC	
NSAID	Diclofenac	NDC	
NSAID	Salicylates	NDC	
NSAID	Etodolac	NDC	
NSAID	Fenoprofen	NDC	
NSAID	Flurbiprofen	NDC	
NSAID	Ibuprofen	NDC	
NSAID	Indomethacin	NDC	
NSAID	Ketoprofen	NDC	
NSAID	Ketorolac tromethamine	NDC	
NSAID	Meclofenamate sodium	NDC	
NSAID	Mefenamic acid	NDC	
NSAID	Meloxicam	NDC	
NSAID	Nabumetone	NDC	
NSAID	Naproxen sodium	NDC	

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NSAID	Oxaprozin	NDC
NSAID	Piroxicam	NDC
NSAID	Sulindac	NDC
NSAID	Tolmetin	NDC
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Oral steroids	Prednisolone	NDC
Oral steroids	Betamethasone	NDC
Oral steroids	Dexamethasone	NDC
Oral steroids	Hydrocortisone	NDC
Oral steroids	Methylprednisolone	NDC
Oral steroids	Deflazacort	NDC

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Phototherapy history was defined using Current Procedural Terminology (CPT) codes. Medications used during the lookback period were identified in pharmacy dispensation claims using National Drug Codes (NDC).

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**Table S3.** Additional characteristics of psoriasis or psoriatic arthritis patients at the time of index date, overall and by drug class.

	All (n=11,560)	IL-17 (n = 2,148)	IL-12/23 (n = 2,882)	TNF (n = 6,530)
Geographic area				
Metropolitan	10,393 (90%)	1,968 (92%)	2,619 (91%)	5,806 (89%)
Micropolitan	650 (6%)	93 (4%)	147 (5%)	410 (6%)
Small town core & rural	517 (5%)	87 (4%)	116 (4%)	314 (5%)
Health plan				
Exclusive Provider				
Organization	1,297 (11%)	230 (11%)	349 (12%)	718 (11%)
HMO	974 (8%)	194 (9%)	207 (7%)	573 (9%)
Other	189 (2%)	34 (2%)	31 (1%)	124 (2%)
Point-of-Service	9,100 (79%)	1,690 (79%)	2,295 (80%)	5,115 (78%)
Race				
Asian	456 (4%)	92 (4%)	128 (4%)	236 (4%)
Black	728 (6%)	132 (6%)	154 (5%)	442 (7%)
Hispanic	1,215 (11%)	236 (11%)	326 (11%)	653 (10%)
White	9,161 (79%)	1,688 (79%)	2,274 (79%)	5,199 (80%)
Education level				
Up to high school	2,633 (23%)	486 (23%)	640 (22%)	1,507 (23%)
Bachelor's degree	6,464 (56%)	1,189 (55%)	1,570 (55%)	3,705 (57%)
Graduate training	2,463 (21%)	473 (22%)	672 (23%)	1,318 (20%)
Diagnosis in lookback period				
Ankylosing spondylitis	215 (2%)	34 (2%)	20 (1%)	161 (3%)
Chronic pulmonary disease	823 (7%)	151 (7%)	175 (6%)	497 (8%)
Peripheral vascular disorders	136 (1%)	27 (1%)	37 (1%)	72 (1%)
Cardiac arrhythmias	379 (3%)	72 (3%)	87 (3%)	220 (3%)
Congestive heart failure	102 (1%)	20 (1%)	26 (1%)	56 (1%)
Depression	1,277 (11%)	240 (11%)	280 (10%)	757 (2%)
Diabetes, uncomplicated	1,175 (10%)	277 (13%)	261 (9%)	637 (10%)
Diabetes, complicated	585 (5%)	153 (7%)	136 (5%)	296 (5%)
Hypertension	2858 (25%)	605 (28%)	640 (22%)	1613 (25%)
Liver disease	438 (4%)	89 (4%)	114 (4%)	235 (4%)
Obesity	1229 (11%)	257 (12%)	262 (9%)	710 (11%)
Renal failure	146 (1%)	31 (1%)	31 (1%)	84 (1%)
Emergency room visits				
0	10,212 (88%)	1,895 (88%)	2,573 (89%)	5,744 (88%)
1	998 (9%)	199 (9%)	241 (8%)	558 (9%)
2 or more	350 (3%)	54 (3%)	68 (2%)	228 (4%)

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Hospitalized	315 (3%)	45 (2%)	63 (2%)	209 (3%)
Physician office visits	5 (3)	5 (3)	4 (3)	5 (3)
Specialist office visits	2 (1)	2 (1)	2 (2)	2 (1)

Continuous variables are presented as mean (standard deviation), and categorical variables are presented as counts (percentages).

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**Table S4.** Additional characteristics of psoriasis patients at the time of index date, overall and by drug class.

<b>Variable</b>	<b>Overall (n=9692)</b>	<b>IL-17 (n = 1903)</b>	<b>IL-12/23 (n = 2644)</b>	<b>TNF (n = 5145)</b>
Age	46.09 (12)	48.02 (11)	45.59 (12)	45.64 (12)
Male	5,286 (54%)	1046 (55%)	1465 (55%)	2775 (54%)
Geographic area				
Metropolitan area	8761 (90)	1749 (92%)	2405 (91%)	4607 (90%)
Micropolitan area core	510(5%)	78(4%)	132(5%)	300(6%)
Small town core	269(3%)	54(3%)	66(3%)	149(3%)
Rural areas	152(2%)	22(1%)	41(2%)	89(2%)
Health plan				
Exclusive				
Provider	1044(11%)	195(10%)	308(12%)	541(10%)
Organization				
HMO	773(8%)	165(9%)	185(7%)	423(8%)
Other	162(1%)	30(2%)	28(1%)	104(2%)
Point-of- Service	7713(80%)	1513(80%)	2123(80%)	4077(79%)
Race				
Asian	405(4%)	86(4%)	122(5%)	197(4%)
Black	610(6%)	116(6%)	139(5%)	355(7%)
Hispanic	1045(11%)	206(11%)	302(11%)	537(10%)
White	7632(79%)	1495(79%)	2081(79%)	4056(79%)
Education level				
Bachelor Degree Plus	2129(22%)	438(23%)	626(24%)	1065(21%)
high school or lower	2227(23%)	435(23%)	596(22%)	1196(23%)
less than bachelor	5336(55%)	1030(54%)	1422(54%)	2884(56%)
Household Income				
<\$40,000	1155(12%)	245(13%)	309(12%)	601(12%)
\$40,000-\$74,999	2334(24%)	411(22%)	615(23%)	1308(25%)
\$75,000- \$124,999	3080(32%)	598(31%)	855(32%)	1627(32%)
\$125,000- \$199,999	1821(19%)	376(20%)	493(19%)	952(19%)
\$200,000+	1302(13%)	273(14%)	372(14%)	657(13%)
Diagnosis				
Psoriatic arthritis	3648 (38%)	699 (37%)	650 (25%)	2299 (45%)
Charlson Comorbidity Index score				
0	7011(72%)	1276(67%)	1998(76%)	3737(73%)



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1	1788(18%)	423(22%)	422(16%)	943(18%)
>=2	893(9%)	204(11%)	224(9%)	465(9%)
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Diagnosis in lookback period				
Ankylosing spondylitis	130(1%)	24(1%)	13(1%)	93(2%)
Chronic pulmonary disease	658(7%)	133(7%)	152(6%)	373(7%)
Peripheral vascular disorders	106(1%)	24(1%)	34(1%)	48(1%)
Cardiac arrhythmia s	306(3%)	61(3%)	78(3%)	167(3%)
Congestive heart failure	82(1%)	17(1%)	23(1%)	42(1%)
Depression	1050(11%)	206(11%)	257(10%)	587(11%)
Diabetes	966(10%)	242(13%)	232(9%)	492(10%)
Diabetes, complicate d	479(5%)	132(7%)	114(4%)	233(5%)
Hypertension	2334(24%)	525(28%)	576(22%)	1233(24%)
Liver disease	363(4%)	77(4%)	106(4%)	180(4%)
Obesity	975(10%)	217(11%)	220(8%)	538(11%)
Renal failure	125(1%)	26(1%)	29(1%)	70(1%)
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Emergency room visits				
0	8610 (89%)	1685 (89%)	2373 (90%)	4552 (89%)
1	801 (8%)	173 (9%)	215 (8%)	413 (8%)
>=2	281 (3%)	45 (2%)	56 (2%)	180 (4%)
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Hospitalized	262 (2%)	42 (2%)	52 (2%)	159 (3%)
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Physician office visits				
	4(3)	5(3)	4(3)	4 (3)
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Specialists physician office visits				
	2(1)	2(1)	2 (2)	2(1)
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Number of previous biologics				
0	4918(51%)	275(15%)	1235(47%)	3408(66%)
1	3051(32%)	705(37%)	1022(39%)	1324(26%)
>=2	1723(18%)	923(49%)	387(15%)	413(8%)
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DMARDs in past 6 mos				
Methotrexate	1524(16%)	202(11%)	293(11%)	1029(20%)
Apremilast	694(7%)	200(11%)	217(8%)	277(5%)
Others	404(4%)	64(3%)	86(3%)	254(5%)

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Any steroids use, %	3194(33%)	623(33%)	794(30%)	1777(34%)
NSAIDs prescribed in past 6 months	1176(12%)	225(12%)	224(9%)	727(14%)
Phototherapy in past 6 months	248(3%)	36(2%)	88(3%)	124(2%)

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**Table S5.** Additional characteristics of psoriatic arthritis patients at the time of index date, overall and by drug class.

<b>Variable</b>	<b>Overall (n=5520)</b>	<b>IL-17 (n = 944)</b>	<b>IL-12/23 (n = 889)</b>	<b>TNF (n = 3687)</b>
Age	47(11)	49(10)	48 (11)	46(11)
Male	2626(48%)	440(47%)	417(47%)	1769(48%)
Geographic area				
Metropolitan area	4925(89%)	861(91%)	806(91%)	3258(88%)
Micropolitan area core	331(6%)	46(5%)	45(5%)	240(6%)
Small town core	172(3%)	22(2%)	28(3%)	122(3%)
Rural areas	92(2%)	*	*	67(1%)
Health plan				
Exclusive Provider Organization	606(11%)	103(11%)	100(11%)	403(11%)
HMO	516(9%)	89(9%)	80(9%)	347(9%)
Other	99(2%)	*	*	73(2%)
Point-of-Service	4299(78%)	739(78%)	696(78%)	2864(78%)
Race				
Asian	175(3%)	41(4%)	26(3%)	108(3%)
Black	322(6%)	47(5%)	46(5%)	229(6%)
Hispanic	536(10%)	99(11%)	98(11%)	339(9%)
White	4487(81%)	757(80%)	719(81%)	3011(82%)
Education level				
Bachelor Degree Plus	1137(21%)	200(21%)	204(23%)	733(20%)
high school or lower	1239(22%)	204(22%)	194(22%)	841(23%)
less than bachelor	3144(57%)	540(57%)	491(55%)	2113(57%)
Household Income				
<\$40,000	639(12%)	115(12%)	95(11%)	429(12%)
\$40,000-\$74,999	1326(24%)	197(21%)	215(24%)	914(25%)
\$75,000-\$124,999	1769(32%)	314(33%)	261(29%)	1194(32%)
\$125,000-\$199,999	1036(19%)	184(19%)	175(19%)	677(18%)
\$200,000+	750(14%)	134(14%)	143(16%)	473(13%)
Psoriasis	3648 (66%)	699 (74%)	650 (73%)	2299 (62%)

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Charlson Comorbidity Index score				
0	3656(66%)	569(60%)	577(65%)	2510(68%)
1	1216(22%)	240(25%)	199(22%)	777(21%)
>=2	648(12%)	135(14%)	113(13%)	400(11%)
Ankylosing spondylitis	169(3%)	27(3%)	16(1%)	126(3%)
Chronic pulmonary disease	449(8%)	80(9%)	72(8%)	297(8%)
Peripheral vascular disorders	71(1%)	*	*	46(1%)
Cardiac arrhythmias	206(4%)	39(4%)	35(4%)	132(4%)
Congestive heart failure	54(1%)	*	*	33(1%)
Depression	686(12%)	122(13%)	102(12%)	462(13%)
Diabetes, uncomplected	627(11%)	145(15%)	106(12%)	376(10%)
Diabetes, complicated	312(6%)	83(9%)	60(7%)	169(5%)
Hypertension	1514(27%)	297(31%)	239(27%)	978(26%)
Liver disease	243(4%)	47(5%)	42(5%)	154(4%)
Obesity	700(13%)	146(15%)	112(13%)	442(12%)
Renal failure	87(2%)	21(2%)	12 (1%)	54(1%)
Emergency room visits				
0	4810(87%)	821(87%)	776(87%)	3213(87%)
1	507(9%)	93(10%)	82(9%)	332(9%)
>=2	203(4%)	30(3%)	31(3%)	142(4%)
Hospitalized	177 (3%)	24 (3%)	28 (3%)	125 (3%)
Physician office visits	5 (4)	5(4)	5 (4)	5 (3)
Specialists physician office visits	2 (2)	2 (2)	2 (2)	2 (1)
Number of previous biologics				
0	2689(49%)	133(14%)	312(35%)	2244(61%)
1	1726(31%)	320(34%)	371(42%)	1035(28%)
>=2	1105(20%)	491(52%)	206(23%)	408(11%)
DMARDs in past 6 mos	2064(37%)	331(35%)	287(32%)	1446(39%)
Methotrexate	1435(26%)	174(18%)	183(21%)	1078(29%)
Sulfasalazine	237(4%)	21(2%)	27(3%)	189(5%)
Apremilast	401(7%)	125(13%)	95(11%)	181(5%)

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others	254(5%)	59(6%)	33(4%)	162(4%)
Any steroids use, %	2184(40%)	379(40%)	333(37%)	1472(40%)
NSAIDs prescribed in past 6 months	1132(21%)	180(19%)	139(16%)	813(22%)
Phototherapy in past 6 months	56(1%)	*	*	28(1%)

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**Table S6.** Hazard ratios (95% confidence intervals), from sensitivity analysis to restrict to serious infections listed as primary diagnosis on hospital admissions claims.

<b>Total cohort</b>	
IL-17 vs. TNF	0.78 (0.39-1.60)
IL-12/23 vs. TNF	<b>0.45 (0.27-0.75)</b>
IL-17 vs. IL-12/23	1.22 (0.59-2.53)
<b>Psoriasis</b>	
IL-17 vs. TNF	0.62 (0.27-1.39)
IL-12/23 vs. TNF	<b>0.44 (0.26-0.76)</b>
IL-17 vs. IL-12/23	1.03 (0.47-2.25)
<b>Psoriatic arthritis</b>	
IL-17 vs. TNF	0.65 (0.22-1.86)
IL-12/23 vs. TNF	0.43 (0.18-1.02)
IL-17 vs. IL-12/23	1.03 (0.47-2.25)
<b>Biologic-naïve</b>	
IL-17 vs. TNF	1.87 (0.77-4.53)
IL-12/23 vs. TNF	<b>0.35 (0.16-0.80)</b>
IL-17 vs. IL-12/23	3.51 (0.87-14.25)
<b>Biologic experienced</b>	
IL-17 vs. TNF	0.64 (0.32-1.26)
IL-12/23 vs. TNF	0.55 (0.29-1.05)
IL-17 vs. IL-12/23	0.99 (0.46-2.14)

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**Table S7.** Hazard ratios (95% confidence intervals), from sensitivity analysis to narrow permissible prescription gap to 60 days.

<b>Total cohort</b>	
IL-17 vs. TNF	0.84 (0.45-1.57)
IL-12/23 vs. TNF	0.65 (0.42-1.00)
IL-17 vs. IL-12/23	1.09 (0.59-2.04)
<b>Psoriasis</b>	
IL-17 vs. TNF	0.70 (0.34-1.44)
IL-12/23 vs. TNF	<b>0.62 (0.39-0.98)</b>
IL-17 vs. IL-12/23	1.07 (0.53-2.13)
<b>Psoriatic arthritis</b>	
IL-17 vs. TNF	0.65 (0.25-1.69)
IL-12/23 vs. TNF	0.72 (0.37-1.39)
IL-17 vs. IL-12/23	1.07 (0.53-2.13)
<b>Biologics-naïve</b>	
IL-17 vs. TNF	1.62 (0.71-3.67)
IL-12/23 vs. TNF	<b>0.45 (0.22-0.92)</b>
IL-17 vs. IL-12/23	3.06 (0.93-10.00)
<b>Biologics experienced</b>	
IL-17 vs. TNF	0.73 (0.40-1.35)
IL-12/23 vs. TNF	0.83 (0.48-1.45)
IL-17 vs. IL-12/23	0.81 (0.42-1.55)